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# TREATMENT OF ADVANCED CARCINOMA OF THE BREAST*

BY

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Endocrine treatment of carcinoma of the breast has gone through a number of phases from hormonal therapy with androgens, oestrogens, and corticoids to oophorectomy, adrenalectomy, and hypophysectomy, each of which has led on occasion to dramatic improvement but none of which has been shown to be outstandingly the best. It is well known that some tumours of the breast are hormone-dependent while others are not, and that tumours which are hormone-dependent initially will eventually escape from dependence and progress inexorably despite further attempts to alter the hormonal environment. The reasons for these differences are obscure, partly because the factors which are responsible for mammary development and lactation are still not completely understood and partly because hormonal balance is difficult or impossible to assess adequately.

### Hormonal Factors in Breast Development

Knowledge of the hormonal factors responsible for development of the breast has accumulated gradually over the past thirty years, aided particularly by the work of Folley (1956) and his group at Reading and by Lyons (1958) and his colleagues at Berkeley, California. These hormonal factors are now becoming more clearly defined owing to the use of experimental animals whose relevant endocrine glands have all been removed, and also to the use of chemically pure hormones. The hormonal factors are grouped broadly under mammogens and lactogens, terms which are in line with the well-known terms oestrogens, progestogens, and androgens.

Mammogens may be defined as hormones which, acting singly or in synergism with other hormones, will induce any of the three main phases of mammary growth—ductal, ducto-alveolar or lobular, and lactational; and lactogens as hormones which, acting singly or in combination with other hormones, will induce milk formation. The term lactogen therefore has a narrower connotation, and it is noteworthy that lactogenic hormone is itself a mammogen (see Diagram on next page). For this reason Lyons prefers the term mammotrophic hormone (M.T.H.), which is also in line with the other trophic hormones—gonadotrophic, thyrotrophic, and adrenocorticotrophic. Likewise the California group prefer to call growth hormone somatotrophic hormone (S.T.H.). S.T.H. is the other main pituitary mammogen. Both M.T.H. and S.T.H. are available as pure proteins by current standards. Both act on the breast in synergism with steroid hormones.

It is well known that oestrogens promote ductal growth in the breast, but they are quite incapable of preventing ductal atrophy which follows hypophysectomy in the young rat. Lyons has shown conclusively that they are dependent on the presence of S.T.H. to prevent this atrophy. S.T.H. is also incapable of preventing ductal atrophy in the rat which is deprived of its sources of steroidal hormones. The two hormones are therefore said to act in synergism. It is remarkable that substitutes have been discovered for both hormones. The adrenal mineralocorticoid deoxycortone has the same action as oestrone when given in doses five hundred times as great by weight, and smaller amounts enhance the combined action of oestrone and S.T.H. S.T.H. can be replaced by long-acting insulin, but its action is less pronounced (Ahrén and Jacobsohn, 1956; Ahrén and Etienne, 1958).

S.T.H. and oestrogen are incapable of inducing the next stage of development of the breast, but lobular growth will occur in young castrated rats treated simultaneously with the corpus luteum hormone progesterone. This does not occur in the hypophysectomized rat, however, because progesterone, like oestrogen, requires a pituitary hormone as synergist. Lyons has shown that this is M.T.H. There are therefore at least four hormones which are essential for development of the breast up to this stage—oestrogen with S.T.H. and progestogen with M.T.H.—and it is remarkable that the body has no confidence in its ability to produce enough of them for all the requirements of pregnancy. As a result high concentrations of at least three are produced in the placenta, the production of S.T.H. by this organ being still questionable. It is interesting to speculate on the influence of this factor on carcinoma of the breast. Finally, in the rat which has been deprived of its pituitary, gonads, and adrenal glands the addition of an adrenal glucocorticoid like cortisol leads to better development, but still no milk is formed. Curiously, the thyroid gland appears to be unimportant for this development.

### Milk Secretion

In the experimental rat, milk secretion depends on the continuation of treatment with M.T.H. and the withdrawal or great reduction of treatment with the sex steroids oestrogen and progestogen. In an animal deprived of its adrenal glands and gonads the addition of corticotrophin or a glucocorticoid like cortisol is essential. Six hormones are therefore ultimately necessary for the production of milk. The transfer of milk from the lobules to the larger ducts is initiated by the posterior pituitary hormone oxytocin, and the suckling stimulus is necessary for its delivery. Suckling probably causes the secretion of oxytocin.

Throughout the development of the breast the ratio of these various hormones to one another is important and is variable from species to species. For instance, in the oophorectomized goat whose pituitary is left intact oestrogen alone in suitable doses can cause extensive development of the udder with lactation, so that progesterone appears to be relatively less important in this species. The ratios of the hormonal factors required for the development of the human breast have still to be established, and clearly these may be of considerable value in the study of carcinoma of the breast.

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### Oestrogens in Relation to Carcinoma

The conception of hormone-dependence of a carcinoma implies that the qualitative character or absolute or relative concentration of certain hormones is important for neoplastic growth, and extensive studies have been made of the concentration of various hormones in blood and urine in an attempt to correlate them with remissions or relapses of the disease. The oestrogens have received most attention partly because the various surgical procedures have been designed primarily to remove the source of oestrogens and partly because there are well-recognized methods for their measurement. The results of a number of investigations on urinary oestrogens were described in a series of papers read at a Conference on Endocrine Aspects of Breast Cancer held at the University of Glasgow in 1957 and published in its *Proceedings*. The methods are, however, by no means simple. There are two ways of dealing with them—by biological assay and by chemical determination.

At first sight the biological method would seem to be the method of choice because it is sensitive and it measures the total biological activity of oestrogens regardless of the

| | Terminology | Anterior Pituitary Hormones | Ovarian Steroid Hormones | Auxiliary Hormones |
|---|---|---|---|---|
| Mammogen | Ductal growth | Growth or somatotrophic hormone (S.T.H.) | Oestrogen (e.g., Oestrone) | Corticotrophin or mineralocorticoid (e.g., deoxycortone) |
| Mammogen | Ducto-alveolar or lobular growth | Lactogenic or mammotrophic hormone (M.T.H.) | Progestogen (e.g., Progesterone) | Corticotrophin or glucocorticoid (e.g., cortisol) |
| Lactogen | Lactation | Lactogenic or mammotrophic hormone (M.T.H.) | None | Corticotrophin or glucocorticoid (e.g., cortisol) (obligatory) |
| | "Let down" | Posterior pituitary hormone Oxytocin | Suckling — | — stimulus |

potency of individual chemical entities. Unfortunately it is necessary first to extract the oestrogens from urine, and the chemical procedures involved may lead to the inactivation of some oestrogenic substances, and also to the activation of some previously non-oestrogenic substances. Moreover, there are substances in urine, like androsterone, which, although not oestrogenic themselves, augment the action of oestrogens in certain assays, and sometimes there are also substances which inhibit the action of oestrogens. We spent a considerable amount of time investigating the biologically active oestrogens and their augmentors and inhibitors in the urine of patients with carcinoma of the breast both before and after operations, including oophorectomy, adrenalectomy, and hypophysectomy. We did not publish our results because we felt that a great deal more academic research was required first in order to elucidate these problems.

If we accept the limitations of the methods, however, we would agree with Scowen (1958) that there appears to be no correlation between the amount of residual oestrogen assayed biologically in urine and the progression or remission of metastatic carcinoma of the breast after endocrine surgery. Indeed, we have been impressed with one patient on whose urine we did a large series of investigations. It consistently contained biologically measurable amounts of oestrogens for nine months after completion of bilateral oophorectomy and adrenalectomy. During this time she had an excellent remission. Then simultaneously with the onset of a relapse the oestrogens disappeared from her urine and were never detectable again.

A method for the chemical determination of the three oestrogens—oestrone, oestradiol-17$\beta$, and oestriol—has been developed by Brown (1955) which is satisfactory for the concentrations found in the urine of women during the reproductive phase of life. Subsequently it was modified for use with urine of low oestrogenic concentration by Brown, Bulbrook, and Greenwood (1957a, 1957b). Using this procedure, Brown (1958) found that there was no significant difference in the excretion of these three oestrogens by women who had passed the menopause, whether they had carcinoma of the breast or not, and Bulbrook and Greenwood (1957) showed that oophorectomy and adrenalectomy or hypophysectomy (Greenwood and Bulbrook, 1957) in younger women caused a big reduction in excretion, but often failed to abolish it. No comprehensive analysis is available of the relationship between the amount of these oestrogens excreted and the remission or progression of the carcinoma. Perhaps such an analysis would be premature because of the shortcomings of the methods. They do not measure certain other known oestrogens which may be present in significant amounts in urine, like 16-epioestriol, 16$\alpha$-hydroxyoestrone, or 2-methoxyoestrone, and studies with radioactive oestrogens indicate that all the known oestrogens represent only a fraction of the total metabolites (Beer and Gallagher, 1955), but apparently they do measure other substances which are not biologically active oestrogens.

Diczfalusy, Birke, Franksson, Hellström, Hultberg, Plantin, and Westman (1958) attempted to characterize substances extracted from the urine of three patients with carcinoma of the breast after bilateral oophorectomy and adrenalectomy. They obtained two substances which behaved like oestrone and like oestradiol-17$\beta$ with Brown's procedure, but they behaved quite differently in studies of counter-current distribution and there was a gross discrepancy between the amount of each substance extracted and its biological activity. It is apparent, therefore, that, as in the case of the biological assay, a great deal more fundamental research is needed into the chemistry of the oestrogens and similar substances before the relationship between the production of oestrogens and carcinoma of the breast can be settled.

### Progesterone ; 17-Ketosteroids

A considerable amount of attention has been devoted to other steroids. Progesterone, which plays such an important part in the development of the breast, cannot be measured in blood or urine as a routine procedure. Some 20% of circulating progesterone is converted into an inert and more readily soluble steroid, pregnanediol, and a satisfactory method has been developed for its determination in urine (Klopper, Michie, and Brown, 1955). Unfortunately other steroids, including adrenocortical steroids, are also partly converted into pregnanediol, but the amount excreted in urine is commonly regarded as a good reflection of the level of circulating progesterone. Pregnanediol disappears from urine after oophorectomy and adrenalectomy (Strong, Brown, Bruce, Douglas, Klopper, and Loraine, 1956), and its absence is probably a good indication of complete ablation of glandular tissue. No attempt has been made to use this procedure as an indication of hormone dependence in carcinoma of the breast.

The 17-ketosteroids have also received attention. They constitute a conglomeration of substances whose only common denominator is a ketone in position 17 of the steroid nucleus. Some of them are biologically inert, others are androgenic, and yet others have widely different endocrine activities. Measured as a group they are of little or no clinical value now that better and more specific procedures have been developed, especially for the measurement of adrenocortical function. Various methods have been developed for the subdivision of neutral 17-ketosteroids into smaller groups which can be measured separately or for the isolation of individual members of the groups.

A number of workers have applied these procedures to the urine of patients with carcinoma of the breast, but only one group has claimed to show significant differences in

excretion between patients who respond to glandular ablation and those who do not. In a preliminary report Allen, Hayward, and Merivale (1958) showed that the ratio of 11-deoxy-17-ketosteroids to 11-oxy-17-ketosteroids is reduced in patients who subsequently fail to respond to oophorectomy and adrenalectomy or to hypophysectomy. This work has been criticized by Kellie (1958) on the grounds that the method which they employed gives rise to artifacts, and certain 11-hydroxylated 17-ketosteroids are hydrated and appear in the 11-deoxy group. Moreover, Plantin, Birke, Diczfalusy, Franksson, Hellström, Hultberg, and Westman (1958), in a similar investigation, found no such differences. If the work of the group at Guy's Hospital is eventually confirmed it would be of considerable clinical value in helping to decide which patients are most suitable for endocrine surgery, and further results are awaited with interest.

### Pituitary Hormones

There remains a group of pituitary hormones which play various parts in the development of the normal breast. They comprise S.T.H., M.T.H., corticotrophin, and the gonadotrophins. Various methods have been developed for the assay of S.T.H. and corticotrophin in extracts from animal pituitary glands, but none is suitable for the routine examination of blood or urine. The assay of M.T.H. in human body fluids is little better. The response of the pigeon-crop gland to injections of urinary extracts has been employed by Coppedge and Segaloff (1951) as a measure of M.T.H. Using this method, Segaloff and his co-workers claimed to show changes in the excretion of M.T.H. by patients with cancer of the breast treated with a variety of steroid hormones (Segaloff, Horwitt, Carabasi, Murison, and Schlosser, 1953; Segaloff, Carabasi, Horwitt, Schlosser, and Murison, 1954; Segaloff, Gordon, Carabasi, Horwitt, Schlosser, and Murison, 1954), but it is doubtful if the method is sensitive or reliable enough for clinical use.

Hadfield (1958a) has used the proliferation of the mammary gland of the immature male mouse as an end-point of an assay for what he terms "pituitary mammotrophic substances." The method has been criticized on the grounds that many substances can cause breast development, and there is insufficient evidence about the specificity of this assay. He has partly overcome this difficulty by using hypophysectomized weanling male mice, but very few mice are suitable for the test. He found that only two out of 36 strains examined were satisfactory, and when these two strains were used in another laboratory they were found to have lost their responsiveness (Williams, 1958). Such variation in the sensitivity of a strain to different substances is not uncommon, and sometimes presents considerable difficulty in assay work. The onus lies with the critic to repeat the work until successful. A more serious criticism is that there is insufficient evidence about the precision of the assays performed by Hadfield, but doubtless this information will be forthcoming. Meantime, Hadfield has claimed to be able to demonstrate "mammotrophic substance" in the urine of 57% of women who had passed the menopause and of all younger women during the second half of the menstrual cycle. Recently he (Hadfield, 1958b) has applied the method to the serum of five younger women and found activity in all of them. This work is potentially of such importance in the investigation of cancer of the breast that it warrants considerable effort to repeat it elsewhere.

The assay of urinary gonadotrophins is on rather firmer foundations. The majority of workers use the increase in weight of the uterus of the immature mouse as a measure of the combined effect of follicle-stimulating hormone (F.S.H) and of luteinizing or interstitial-cell-stimulating hormone (I.C.S.H.). Loraine (1958) used this procedure to measure total gonadotrophins excreted by women with carcinoma of the breast who had passed the menopause. He claimed that those who subsequently failed to respond to treatment with stilboestrol excreted significantly more than those who responded to it. Further studies along these lines are awaited with interest. The excretion of urinary gonadotrophins has also been employed as an indication of complete hypophysectomy. We have used the test as a semi-quantitative procedure but our interest has been more concerned with the development of assays capable of demonstrating differences in the relative concentrations of F.S.H. and I.C.S.H. These methods have not yet been applied to the problem of cancer.

### Persistence of Steroids after Gland Ablation

The discovery that various steroids continue to circulate in the blood and to be excreted in the urine after ablation of the glands which secrete them has led to a reappraisal of the methods of treatment and to a reconsideration of their sources of origin. Incomplete removal of the ovaries or adrenal glands is one possible explanation for the persistence of oestrogens and certain other steroids, and the presence of accessory cortical tissue is another. It has been suggested that stimulation with corticotrophin might demonstrate their presence by causing an increased production of steroids, but it is not generally helpful, possibly because the glandular tissue is already working to its maximum capacity. The incidence of such tissue should be known from necropsy studies, but the remnants may easily be missed unless serial sections are made of large areas. Accessory adrenocortical tissue has been estimated by various workers to occur in some 20% of all subjects. Symington, Grant, O'Donnell, Carr, and Forrest (1958) reviewed the literature on this subject and failed to demonstrate such tissue in a very careful examination of their own material at necropsy. It seems to be unlikely that accessory adrenal glands are a common source of persisting steroids after adrenalectomy, and their origin must be sought elsewhere, possibly from exogenous sources.

The failure of hypophysectomy to relieve all patients with carcinoma of the breast may be due to the presence of accessory anterior pituitary tissue in the roof of the pharynx. This subject has been reviewed by Müller (1958), who found a pharyngeal pituitary consistently in all his own material at necropsy. Its functional significance is uncertain. It contains chromophobe and eosinophil cells and is known to have been the site of an eosinophilic tumour associated with acromegaly. It contains no basophil cells, which might explain the absence of urinary gonadotrophins after hypophysectomy, while S.T.H. and M.T.H. might continue to be produced by the pharyngeal remnant. Ultimately its significance must be established by the development of methods for the assay of the hormones which it produces.

In conclusion we are faced with this challenge. Empirical surgery has established the existence of hormone-dependent carcinoma, and all the biologists, chemists, and pathologists together have so far been unable to explain it.

### Summary

Growth hormone acts synergistically with oestrogen to cause ductal growth, and lactogenic hormone acts synergistically with progestogen to cause lobular growth in the breast of immature rats deprived of their pituitary and steroid-producing glands. Little is known, however, of the concentrations of these hormones required for normal breast development in the human subject, but it seems likely that they all may play some part in the development of hormone-sensitive types of breast cancer.

There are several important technical factors which detract from the value of biological and chemical estimations of the various hormone concentrations in blood and urine, and, so far, no convincing correlation has been demonstrated between the remission or progression of cancer and the residual excretion of oestrogens or other steroids. The assay of growth and lactogenic hormones in body fluids is not practicable as a routine procedure at the present time.

The remarkable clinical improvement of patients with breast cancer which sometimes follows hypophysectomy or adrenalectomy and oophorectomy is still not satisfactorily explained.


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# AN ANALYSIS OF 161 CASES OF CARDIAC INFARCTION WITH ABC ELECTROCARDIOGRAPHIC STUDIES AND 36 NECROPSIES*


BY

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In the *Lancet* (1954), in a section concerning vectorcardiography and referring to the ABC display, it was stated that "satisfactory electrocardiograms have been obtained from cases of known heart disease, but confirmation from larger numbers is needed." In the present paper 161 cases of cardiac infarction observed over a period of 2–8 years by the ABC display have been studied with this end in view. Necropsies were performed on 36 cases of this series.

The standard unipolar limb and chest leads record electrical activity almost solely in the frontal (coronal) plane. The vectorcardiograph is limited with regard to the study of temporal relationships and the acceptance of a standard frame. This simple three-dimensional display, allowing a three-dimensional analysis, is not deficient in these respects. As will be seen from this survey, it detects all changes detected by the present normal leads, and in addition detects changes not demonstrated by the normal leads.

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The series of patients is classified into the following groups.

A. (i) Clinically diagnostic, standard E.C.G. diagnostic, ABC leads diagnostic: 127 cases; 32 traced deaths, 25 necropsies. (ii) Clinically diagnostic, standard E.C.G. not diagnostic, ABC leads diagnostic: 24 cases; 5 traced deaths, 5 necropsies.

B. Clinically not obvious, standard E.C.G. not diagnostic, ABC leads diagnostic: (i) fatal cases 4, 2 necropsies. (ii) survivors 2.

C. Infarct totally unexpected, ABC leads diagnostic: 1 case (necropsy positive).

D. Clinical diagnosis infarction, ABC leads negative: 1 case (necropsy negative).

E. Special instances: (i) Minor infarct patterns: 4 cases; 1 traced death, 1 necropsy. (ii) Abnormal T-wave form (also included in A): 1 case. (iii) heart block (also included in A): 17 cases; 12 traced deaths, 9 necropsies.

## Method

The majority of the patients were examined personally by me, and the condition of all patients was discussed with at least one physician concerned with the management of each patient.

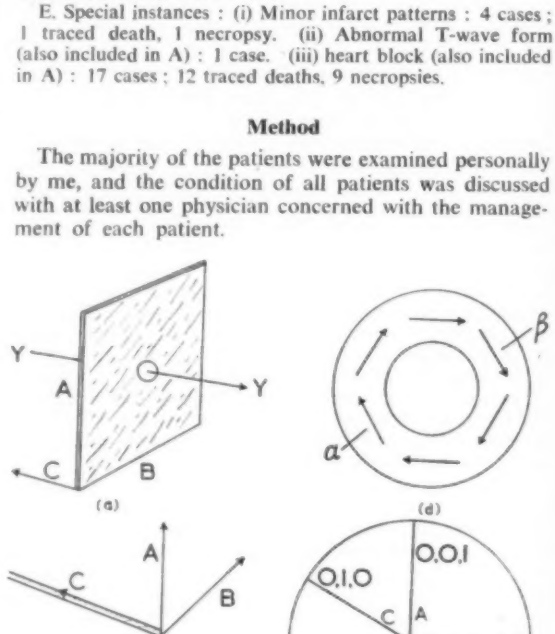



FIG. 1.—(*a*) Planar sheet (diagrammatic) of infarction AB at right-angles to YOY. Further details in text. (*b*) Linear infarction, C, at right-angles to A and B axis. Further details in text. (*c*) Four dipoles paired and orientated at 180 degrees. Further details in text. (*d*) Clockwise dipoles. Further details in text. (*e*) Direction cosines (0,0,1; 1,0,0; 0,1,0) to ABC axis. Further details in text.

E.C.G. recording was usually performed with a Both direct writing electrocardiograph and in some instances with a "cardio-scribe" direct writing machine. A continuous check was made to ensure that the recording apparatus was kept in good condition.

When patients died every endeavour was made to have a necropsy performed, though this was not always possible owing to conditions beyond our control. In some instances the freshly removed intact heart was perfused through the coronary vessels with a gelatin–barium suspension at 37° C. and 120 mm. Hg pressure and then *x*-rayed as described by Blumgart *et al.* (1940).

ABC electrocardiographic recording was made from the right-angled system: xiphisternum (X), manubrium

sterni (M), left axilla (L), and right chest at the base (R), as described previously (Trethewie, 1953). Lead A is taken from the manubrium and xiphisternum (MX), lead B from the left mid-axilla at the level of the xiphisternum and the xiphisternum (LX), lead C from the right chest at the base at the level of the xiphisternum and the xiphisternum (RX). LX, MX, and RX are all mutually at right angles. The electrode connected to X is positive for upward deflection and thus corresponds to the left leg lead in lead II Einthoven. Thus the right arm lead corresponds to the varying electrode placed successively on the manubrium, left axilla, and right chest at the base. This should define electrical fields in a three-dimensional conductor when these fields emanate from a dipole within the volume, and probably also would analyse whatever combinations of dipoles are present or whatever the characteristic electrical events arising in the conductor. Certain modifications occur owing to the fact that the medium is not homogeneous, though nearly so, and the conductor is not infinite, but bounded by the body surface. The former modification is regarded as minor by most observers. Schmitt (1955) has shown there is a modification, and actually recorded it, with a homogeneous medium containing a dipole inside a model in the shape of the human torso.

**Influence of Infarction on the E.C.G.**

Let us consider a planar sheet of heart muscle which is infarcted (Fig. 1,a). Such a sheet produces a "current of injury," the injured portion of muscle being at the surface electrically negative compared with the surface of the adjacent healthy muscle. The QRST complex then shows elevation of the RT segment, provided the leads chosen are in the plane of the affected muscle (AB). In the line YOY, at right angles to this plane for all practical purposes, the heart contains only healthy muscle, and segment elevation will not be observed in a lead chosen along this direction—for example, lead C (Fig. 1,a). Depending on the angle formed by the planar sheet to the directions A, B, and C, so we will obtain more or less "weighting" or segment elevation in specific leads.

Let us next consider a linear distribution of infarction (Fig. 1,b). In this instance no effects will be detected in leads A, B, but considerable change will be detected in lead C. If C were only slightly askew to the plane AB there would be relatively little observable effects of the infarction in C. This is the case with $V_{1-3}$ with small septal infarcts. Such infarcts do, however, show gross changes in lead C of the ABC display.

Since the posterior aspect of the heart forms a considerable vertical sheet of muscle, infarcts in this area classically produce maximal effects in lead A. The antero-lateral aspect of the left ventricle which recedes posteriorly and cranially is parallel to lead B, and thus infarcts in this region produce maximal changes in that lead. The septum is almost parallel to lead C, and infarcts in this portion in the heart produce maximal effects in lead C. Likewise the AC pattern indicates posterior septal infarction and the BC pattern indicates anterior septal infarction. This aspect is amplified later with necropsy studies (cf. Fig. 2).

To produce a null effect as referred to above, dipoles would be required to be orientated in opposite directions (Fig. 1,c). However, cardiac infarction simply produces a steady state of "injury" current which gradually subsides over two to three weeks with the development of fibrosis followed by contraction. This latter phenomenon alters the axis of adjacent healthy muscle fibres and may result in a permanent inversion of the T wave in a particular lead. Ischaemia may also affect the T wave. Two areas of infarction would summate this "negativity," not cancel each other out. Similarly a null effect could be produced by a ring of muscle with a clockwise (or anti-clockwise) orientation of dipoles, and dipole $\alpha$ and dipole $\beta$ (Fig. 1,d) might then cancel out one another; but again the effect of infarction, as before, is to produce

FIG. 2.—Infarct sites, as detected at necropsy. Continuous line, recent infarction; broken line, discrete fibrosis; dotted line, degeneration only. Top left-hand corner, Patient number, E.C.G. infarct pattern designated centrally.

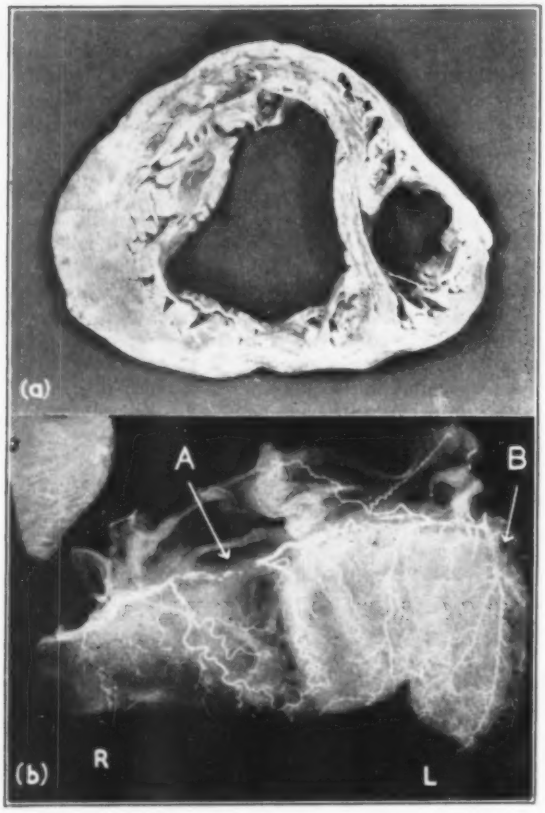



FIG. 3.—(*a*) Patient 93: Septal infarction extending anteriorly over the left ventricle with fibrotic lamina from older infarction parallel to the right. Further details in text. (*b*) Roentgenogram of perfused heart from Patient 128. Right coronary block at A and left coronary at B. Further details in text.

a steady "state" of negativity. Contraction of infarcted muscle does not occur with heart beats. In the presumed circus movement of flutter, now not acceptable in its original form, the repetitive firing of the P wave is the diagnostic feature, not injured muscle. Further, the nearer bipolar leads are to the heart the less likely is it that clockwise dipoles would cancel one another out. The ABC leads are close to the heart.

For changing potentials—that is, when currents are produced as distinct from static charge—the field patterns will not be arrived at immediately because there is a degree of impedance in the conductor (that is, the body). However, Kaufman and Johnston (1943) consider these variations in resistance as minor, and that they do not influence potentials greatly. Further preliminary tests on a human torso with a dipole source at the heart position show that the potentials as recorded for leads A, B, and C, while not being at the precise level expected, are nevertheless at 60%, 75%, and 90% of the theoretical value, and, so long as an abnormal contour appears even in part, this should be large enough to have practical significance. Again the particular problem concerning us here is the evaluation of infarcts, and these produce a steady current of injury, so that estimates based on static laws probably do apply here. The problem is best answered by the practical results obtained: namely, do the leads used record significant changes in accord with pathological findings?

It would appear axiomatic that a right-angled distribution of the ABC type is the logical display to choose for electrocardiography because no electrical axis is then unrepresented and more obvious segment elevation must be produced in one lead than is the case with any other display owing to that distribution. In the representation shown in Fig. 1,e, the direction cosines become 0,0,1; 0,1,0,; and 1,0,0, when the ABC leads correspond to the axes chosen in the original figure, because cos 90° = 0 and cos 0° = 1. The approximate size of the infarct can then be indicated. In point of fact point X (xiphisternum) is close to 0 (Fig. 1,e), since the heart occupies the anterior part of the mediastinum, and this distribution applies as nearly as is possible practically. Further, this distribution, being located on skeletal points—namely, manubrium and xiphisternum—ensures regularity of repetition of the display from patient to patient.

### E.C.G. Pattern and Infarct Site as Revealed at Necropsy

The sites of the infarct in 36 instances where necropsy studies were available are shown in Fig. 2. In these the heart has been cut across horizontally below the level of the atria and observed from above, so that the left ventricular cavity appears on the left and the right cavity on the right. The photographic findings of the heart from Patient 93 are shown in Fig. 3,a, where two parallel septal infarcts of different age are well shown. Leads ABC showed a "Cb" type cardiac infarction, indicating recent septal involvement extending on to the antero-lateral surface. Also $R_A$ was absent and without segment elevation in A—that is, QA form—indicating older infarction in the posterior portion, and in fact there was older septal infarction extending posteriorly to involve both ventricles at a lower level than that shown in Fig. 3,a. It will be observed that, as expected from theory (Trethewie, 1953), "C" type infarcts are largely septal (Fig. 2), "B" type infarcts more commonly involve the antero-lateral aspect (Fig. 2), and "A" type infarcts more commonly involve the posterior aspect of the heart (Fig. 2). Occasionally BC type infarcts involve the posterior and medial aspect of the left ventricle rather than being anteroseptal, especially if block is present. Thick black lines indicate recent cardiac infarction, interrupted lines old infarction (with fibrosis), and dotted lines degeneration only (Fig. 2).

### X-ray Studies: Radio-opaque Perfusion

In five instances the heart was perfused with radio-opaque material, laid open by incision along the anterior border between the two ventricles, the septum excised, and the whole *x*-rayed. Fig. 3b was obtained from Patient 128, and a block is shown in the right coronary artery (A) after giving off the inferior interventricular branch and also in the anterior descending branch of the left coronary artery (B). The E.C.G. (Fig. 4) indicated old posterior infarction ($Q_A$) and recent antero-lateral infarction involving the septum ($ST_{BC}$). At necropsy there was an old posterior infarct, and in the postero-medial aspect of the left ventricle (including the septum) there was recent infarction—that is, parallel, but posterior to the region suggested.

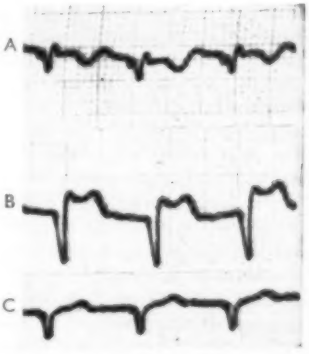



FIG. 4.—E.C.G. of Patient 128, heart depicted in Fig. 3: "Bc" type infarct pattern with old $Q_A$.

## Classified Groups

### A. Cardiac Infarction Obvious Clinically

*(i) Patients with histories indicative of cardiac infarction associated with typical electrocardiographic tracings.*—This aspect need only be discussed quite briefly, and it is sufficient to point out that in 127 patients there was no doubt whatever that the E.C.G. standard display ($E_1$, $E_2$, $E_3$; aVR, aVL, aVF; $V_{1-6}$) yielded conclusive evidence of infarction. Leads ABC also yielded conclusive evidence of infarction in all 127. One impressive feature has been the magnitude of the segment elevation in the ABC display, which is frequently greater than that of the standard display, and the fact that changes are so commonly seen in a greater proportion of leads with the former. Definite pattern changes are observed in at least one lead in 100% of cases, in at least two leads in 86% of cases, and in all three ABC leads in 39% of cases. One of the latter is shown in Fig. 5, which is the tracing obtained from Patient 26, who developed sudden substernal pain at rest five days before admission with a very severe recurrence four hours before admission on May 18, 1955. This tracing is recorded as a "CBa" type infarct pattern (Trethewie, 1953)—that is, there are gross changes in leads C and B, though greater in C, and definite but smaller changes in lead A. The infarct is septal and extends on to the antero-lateral surface. This patient developed a second infarction two months later ("Abc" type)—that is, posterior infarction—and he died on the fifth day of the attack. Necropsy was not permitted.

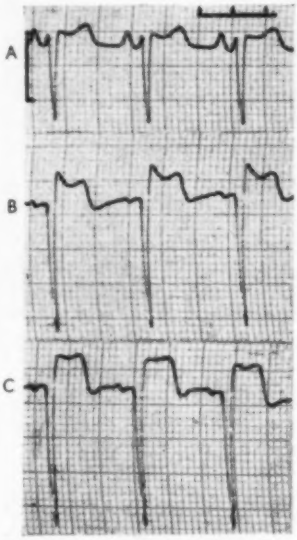



FIG. 5.—E.C.G. of Patient 26: "CBa" type infarct pattern.

*(ii) Patients with histories indicative of cardiac infarction associated with standard display tracings not regarded as indicating evidence of infarction, ABC tracings diagnostic.*—Twenty-four patients (15% of cases) came under this heading. In each case leads ABC yielded unequivocal evidence of infarction. Such an instance is recorded with Patient 106. Three days before admission this patient, a male, complained of the sudden onset of severe pain under the sternum, with collapse. He was sweating, and his colour for a time was somewhat greyish. Twelve days after the onset his B.S.R. was 118 mm. in one hour and 128 mm. in two hours. His standard E.C.G. eight days after the onset is recorded in Fig. 6. The ST segment in $V_{1-3}$ is not quite normal, but this was not regarded as pathognomonic of infarction. The T-wave in $V_5$ and $V_6$ is of low potential and inverted. Leads ABC (Fig. 6), taken at that time, show conclusive evidence of infarction of the Bac type with maximum segment elevation in lead B—that is, antero-lateral cardiac infarction.

The tracing shown in Fig. 7 was obtained from Patient 80, who had attacks of substernal pain on the two days before and on the day of admission to hospital. Four hours before admission the pain was severe, prolonged, and associated with collapse. The standard E.C.G. throughout the course of his illness was recorded as not signifying infarction, but a confident diagnosis of infarction was made on clinical grounds. On the nineteenth day the tracing of leads ABC

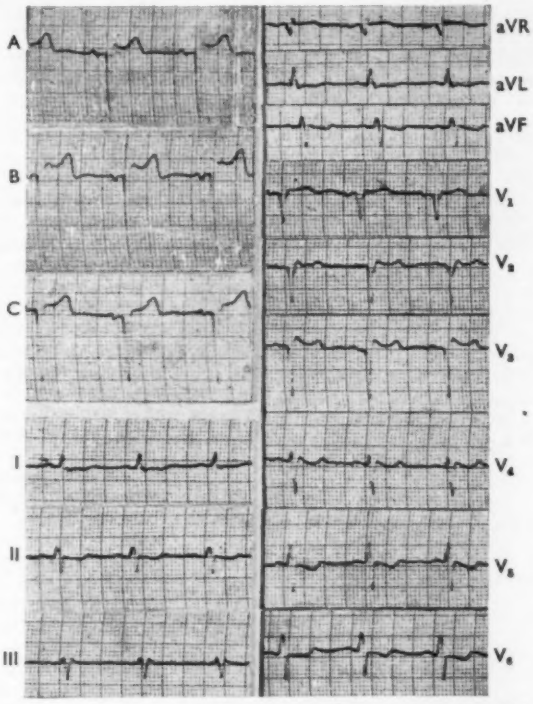



FIG. 6.—ABC-E.C.G. and standard E.C.G. of Patient 106. Tracing taken eight days after onset. Note the considerable segment elevation in B not apparent in standard leads.

was taken (Fig. 7). This shows segment elevation in all leads, maximal in lead B with obvious elevation in lead C with "round-shouldering." Elevation is also present in minor form in lead A. This is the distinctive feature confirming the diagnosis of cardiac infarction in contradistinction to left-heart-strain pattern. In this instance, of course, a confident clinical diagnosis was possible, but the value of electrocardiography, especially if it can be shown to be correct regularly in the absence of a clinical history suggesting infarction, is self-evident, and is discussed in the next section. A similar finding is shown in Fig. 8 (Patient 20), where the tracing was obtained 30 hours after the onset of infarction and segment elevation is considerable, while the standard leads E.C.G. did not indicate infarction.

The infarct pattern in the 24 cases coming under the above heading showed the distribution recorded in Table I.

For clarity, a "BC" infarct pattern—that is, marked change in B and C, though greater in B—includes CB (changes greater in C); likewise with BA and CA, and in 12 instances where some change was observed in the third lead also, the notation was recorded as the two leads in which the changes were greater. It is noteworthy that in only one instance in the 161 patients did lead A (indicative of posterior infarction) yield conclusive evidence of infarction when the standard leads did not. In this case block was present which obscured the diagnosis in the standard leads. This

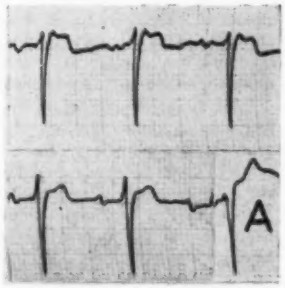



FIG. 7.—E.C.G. of Patient 80, showing typical infarct pattern on the nineteenth day; standard lead tracing not indicative of infarction throughout course of illness.

TABLE I

| Infarct type | BC | BA | B | CA | A |
|---|---|---|---|---|---|
| No. of tracings | 12 | 5 | 4 | 2 | 1 |

aspect will be discussed later. On the contrary, in 14 instances (BC and CA type pattern) where the septum or that portion of the left ventricle parallel to it was involved, conclusive evidence of infarction was manifest in leads ABC, while the standard leads did not yield conclusive evidence of infarction. Of ten patients who died and on whom a necropsy was performed where the pattern was of this type—that is, with major involvement in lead C—the septum was found to be involved in seven, and in three instances the postero-lateral part of the left ventricle (parallel to the septum) was involved. Nine other patients were found to have an associated BA or B type infarct pattern (Table I). Since lead B is inclined at about 40 degrees to the frontal plane, this finding could be expected. Standard lead tracings, where minor changes were observed, which were not regarded as presenting evidence of infarction but were nevertheless not normal, involved leads $V_1$, $V_2$, or $V_3$ in four instances, lead 3 in one, and lead $V_4$ in one. In the remainder changes were quite trivial.

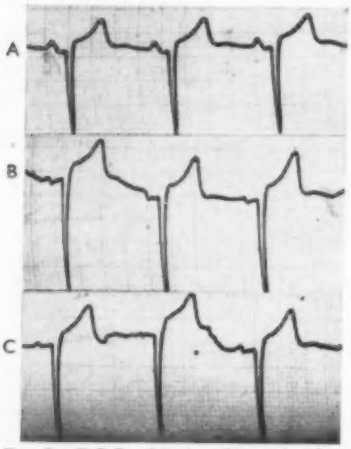


FIG. 8.—E.C.G. of Patient 20; typical infarction 30 hours after onset. Standard leads did not indicate infarction.

Changes found in lead $V_2$ of the type referred to above are probably due to the infarct, but since this lead is only slightly askew to the frontal plane, as referred to earlier, infarct pattern changes are not likely to be marked if the frontal plane leads (Einthoven and lateral V leads) show indefinite infarct patterns.

Five of these 24 patients died. Necropsy was performed on all five subjects, and the infarct was found in the site expected for the ABC finding in each instance.

In 5 of these 24 instances (3% of cases) the initial diagnosis made was of cardiac infarction, but considered opinion at a later date was opposed to this diagnosis. In each instance, in the opinion of at least one other physician and in my own, these patients were still regarded as suffering from myocardial infarction. Such a state of affairs is to be expected, especially as it is recognized that some 15% of patients do not show conclusive evidence of infarction in standard lead electrocardiography. Emphasis in such cases must therefore be placed largely on clinical findings.

It is pointed out below that one patient who was not regarded as suffering from myocardial infarction on clinical grounds, and who was not considered to have a myocardial infarct after necropsy (macroscopic) examination, was recorded as clearly associated with myocardial infarct pattern in the lead ABC findings. Subsequent histological examination of the heart, carried out because of the latter findings, revealed the presence of a laminar infarct in the posterior part of the heart. Again in Section D, below, an infarct was diagnosed clinically without support in the E.C.G. findings with leads ABC; and subsequent necropsy, including microscopical examination, did not reveal the presence of infarction four days later nor was coronary atheroma present. There was also adequate evidence at necropsy for another cause of death. Such findings naturally strengthen one's confidence in the value of leads ABC, and the absence of standard lead confirmation may have played a part in the different clinical opinion expressed in relation to the five patients referred to here. Nevertheless, at the initial examination the clinical picture was regarded by all as being that of cardiac infarction.

The case history of one of these patients is presented as an example.

Patient 53 complained of the sudden onset of tearing pain at the lower end of the sternum and in the epigastrium one week previously. The pain radiated up to the back of the neck. On admission his B.P. was 180/90 mm. Hg. The standard lead E.C.G. was regarded as normal throughout his stay in hospital. Lead 3, obtained on the eighth day after the onset of the pain, showed a minor anomaly considered to be sufficiently like a normal RSR′. The B.S.R. at this time was 35 mm. in one hour and 64 mm. in two hours (Westergren). *X*-ray examination of the lungs was normal. Leads ABC revealed a classical Pardee curve in leads A and C, indicating a postero-septal infarct.

### B. Infarction not Obvious Clinically

*(i) Patients who died where leads ABC showed unequivocal infarction but in whom infarction was not certainly diagnosed on clinical grounds, and the standard leads did not yield definite evidence of infarction.*—Four patients in whom leads ABC showed unequivocal infarction died, while infarction was not certainly diagnosed on other grounds. In each of these patients standard lead E.C.G.s did not confirm infarction. One of the patients had complained for years of abdominal pain on exertion, and, following a more severe attack of pain, dyspnoea at rest appeared. Her B.P. was then 160/120. From a consideration of the clinical picture and the standard E.C.G. leads the consensus of opinion was that the patient suffered from ischaemia. Slight segment elevation was shown in $V_4$, and this was thought not to be indicative of infarction. In leads ABC, however, a classical Bac type infarct pattern was observed—that is, an antero-lateral infarct (Fig. 9). At necropsy an antero-lateral laminar infarct was found in the left ventricle. This infarct encroached neither on the endocardial nor on the pericardial surface. A histological section is shown in Fig. 10, which shows the infarct clearly.

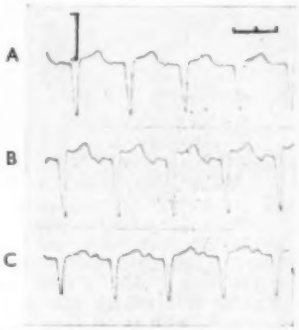


FIG. 9.—Typical "Bac" type infarct. Clinical history thought to indicate ischaemia only. Standard leads, ischaemia; necropsy, antero-lateral infarct (left ventricle).

The second of these patients developed cardiac failure fairly suddenly and was critically ill; it was thought that cardiac infarction could not be excluded. The standard E.C.G. (1, 2, 3, aVL, aVF, $V_2$, $V_4$, $V_6$) did not suggest cardiac infarction, but lead C showed gross segment elevation and also a W-shaped contour, including a well-marked Q wave. At necropsy a recent and an old infarct were found in the septum as expected (lead C lies in the septal axis).

Necropsies were not performed on the other two subjects.

*(ii) Patients who survived where leads ABC showed unequivocal infarction, but in whom infarction was not certainly diagnosed before electrocardiography and the standard leads did not yield definite evidence of infarction.*—There were two patients in this group. One patient, a

woman aged 51, had complained for 15 years of sharp pain near the lower sternum in the evening on walking. She did not stop walking on experiencing the pain. This pain was regarded as not indicative of organic cardiac disease. A standard lead E.C.G. and leads ABC at that time were normal. Her B.P. was 148/80 mm. Hg. Following examination I expressed the opinion that the patient might be suffering from cholelithiasis and advised cholecystography, but that I was not certain whether the patient suffered from angina of effort in addition. Cholecystography revealed the presence of numerous biliary calculi.

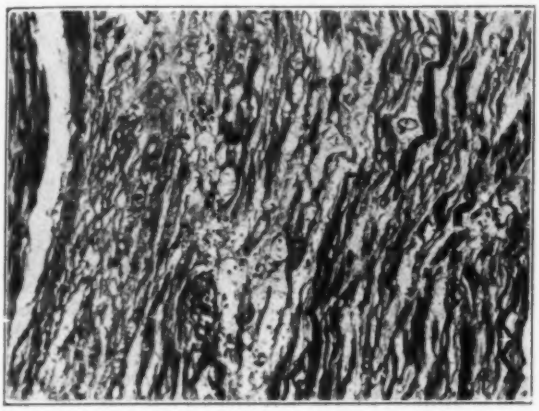


FIG. 10.—Microscopical section of heart from patient whose E.C.G. is recorded in Fig. 9. (×543.)

Cholecystectomy was performed. Two years later the patient stated that the pain had become worse. Then six months later, at a second examination, she said that one week previously she experienced a sudden onset of lower sternal pain and sweated, the pain lasting four hours. A standard lead E.C.G. was normal, but lead A in the ABC display revealed the presence of a classical Pardee curve, indicating posterior cardiac infarction.

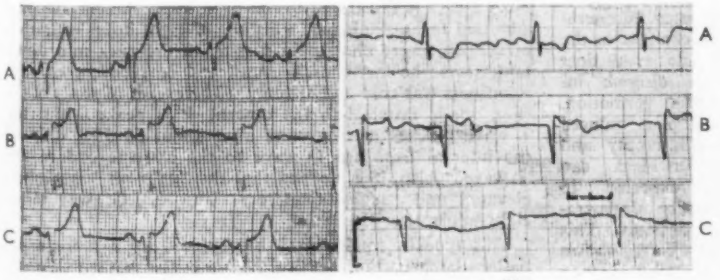
### C. Cardiac Infarction quite Unsuspected on Clinical Grounds but Evident from Leads ABC

This patient was admitted to hospital with hypertension and developed a hemiplegia. He did not complain of cardiac or chest pain. A standard E.C.G. was not done. Leads ABC (Fig. 11a) show segment elevation with round-shouldering in lead A, conclusive evidence of posterior infarction. There is also segment elevation in leads B and C, but in B the elevation is angulated very much as it is in hypertensive strain. With such a degree of elevation in leads B and C in hypertension ordinarily the S waves are much larger. Here they are normal to reduced in potential. The T waves are unduly large and abnormal. The patient was 38 years of age. At necropsy the heart, other than showing considerable hypertrophy, appeared normal macroscopically. However, more careful examination of the posterior part of the heart, carried out because of the ABC-E.C.G. finding, revealed the presence of a recent laminar infarct. The patient was also found to have coarctation of the aorta, and for interest a tracing obtained from another patient who had coarctation of the aorta (without infarction) is shown in Fig. 11b. Interestingly enough the S waves again are not prominent and there is flutter-fibrillation (lead A). Segment elevation with angulation is seen in leads B and C, but, more significantly, the S–T segment is depressed in lead A. This is the distinctive feature of left-heart-strain pattern. With cardiac infarction the S–T segment in lead A is not depressed or concave upwards at the isoelectric line. Infarct patterns with leads ABC always show elevation, not depression, of the S–T segment when this is abnormal. Further, the round-shouldering of the contour is significant of infarction. In the absence of segment elevation, as with other leads, infarction is of course indicated by a cove-shaped usually inverted T wave and a biphasic R–T interval. Segment elevation pattern may conform to the monophasic type or the high take-off of the Pardee type.

### D. Cardiac Infarction Diagnosed Clinically Without Changes in Leads ABC Suggestive of Infarction

This patient complained of shortness of breath and cough for some months and chest pains one week before admission. Retrosternal pain with cyanosis developed on the previous day, and the patient was treated with anticoagulant therapy for cardiac infarction and also treated for cardiac failure, pneumonia, and shock. The prothrombin level fell to 12%.

The standard E.C.G. was recorded as indicating ischaemia only. Leads ABC did not support the clinical diagnosis of cardiac infarction. The ABC-E.C.G. is presented in Fig. 12. Potentials are very low, as is seen sometimes in pericarditis or in approaching death; the T waves are flat. This patient died 72 hours later. The recording made against the ABC leads before death was: "Very low potential, ischaemia apparent in A; I would think the muscle would show degenerative changes microscopically, but the tracing is not of the Pardee type." It was concluded there was no infarction. At necropsy three small foci of old pericarditis were found. The coronary vessels were free of atheroma, as was the proximal aorta. The ventricular muscle was dark brown in colour, but no infarct was found. Microscopical examination at a later date revealed the presence of brown degeneration in the cardiac muscle. Other significant findings at necropsy were gastro-intestinal haemorrhage (gross), pulmonary emphysema, acute bronchiolitis, cholelithiasis, and diverticulitis coli. The gall-bladder was distended with bile and there was impaction of small pigment calculi. If one




(a) (b)

FIG. 11.—(*a*) Typical posterior infarct pattern in patient with coarctation. (*b*) Typical tracing of coarctation of the aorta without infarction.

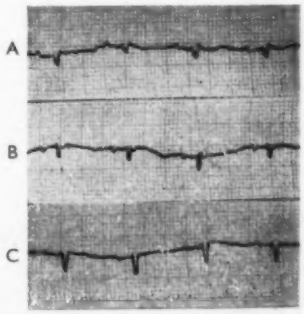



FIG. 12.—E.C.G. of patient with old pericarditis and ischaemia. Further details in text.

C

can apply an electrocardiographic technique which is so complete that infarction can be excluded if the E.C.G. is negative, obviously one has a most valuable tool to aid diagnosis.

### E. Special Instances

*(i) Minor E.C.G. "infarct" patterns.*—It is regarded as likely that, since leads ABC record three leads mutually at right angles with a common origin, the grossness of the infarct can be deduced approximately from the degree of segment elevation all three leads. On the contrary, if only the frontal and slightly skew frontal planes are recorded, gross infarcts may sometimes produce little segment elevation in the electrocardiogram.

A tracing may be observed, in the case of a patient considered to be suffering from cardiac infarction on clinical grounds, where the E.C.G. tracing forms a very small though definite "Pardee" complex or other slight segment elevation. If this tracing is magnified, the evidence of infarction electrocardiographically becomes more obvious. It is suggested such patients developing pain at rest show recent degenerative cardiac changes short of infarction. This feature was observed in four patients in the present series, and is seen more often in private practice. For accuracy of recording, an ink writer forming a fine line, or a cathode-ray oscillograph, is required to demonstrate this feature. Multiple T inversions approaching a cove shape also occur in severe acute ischaemia. All of these patients were diagnosed clinically as suffering from cardiac infarction without any doubt. Three survived. The other patient died. The ABC findings in one of the former showed a Pardee curve in lead B, passing to a cove-shaped inverted T wave and a Pardee curve in lead C. The standard E.C.G. appeared normal, showing an RSR′ of apparently normal type in lead $V_2$. In the remaining two, minor monophasic segment elevation was evident in leads ABC. The ABC findings in the fourth patient showed a curve of Pardee type in lead C, leading to an inverted abnormally shaped T wave. This was less evident in lead B, while there was no segment elevation in lead A (Fig. 13). Magnification of the tracing demonstrated the feature more readily. Similar though less obvious findings were observed in $V_2$ and $V_3$. This patient died seven days after admission on August 22, 1955. The ABC–E.C.G. diagnosis before death was "Pardee type tracing: septal infarct, very small." At necropsy broad zones of pallor were observed in the left side of the interventricular septum and in the papillary muscles of the anterior wall. Both coronary arteries were almost completely occluded at their origins, and elsewhere were grossly atheromatous. Microscopically, cloudy swelling and some vacuolation were seen in the muscle fibres in the pale zone, but no massive infarction was observed (Fig. 14).

It is considered worth while to follow such cases through with necropsy findings wherever possible, so as to determine if such minor changes as illustrated in these four examples are indicative of degenerative changes in the muscle as distinct from discrete infarct formation. Continued reduced blood supply and oxygen lack can be expected to produce degenerative changes. This has been shown for the liver (Trethewie and Gaffney, 1951). Undoubtedly post-mortem changes require exclusion, and the interval after death before necropsy examination needs to be kept at a minimum even though the body is placed in the refrigerator. In view of the facts that the second subject died during cold weather (in Melbourne), was placed in the refrigerator on arrival at the necropsy department, that bands of pallor were seen in the heart in the area suggested to be involved previously by the ABC findings, that the coronary arteries were almost completely occluded at their origins, and that actual vacuole formation was observed in cells in pyriform areas of degeneration, it is considered very likely that the microscopical changes observed in the heart were of ante-mortem origin.

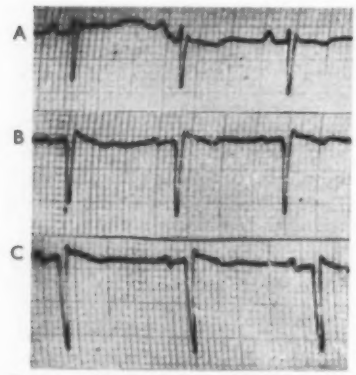



FIG. 13.—Minor infarct pattern of Pardee type. Myocardial degeneration in pyriform areas in septum.

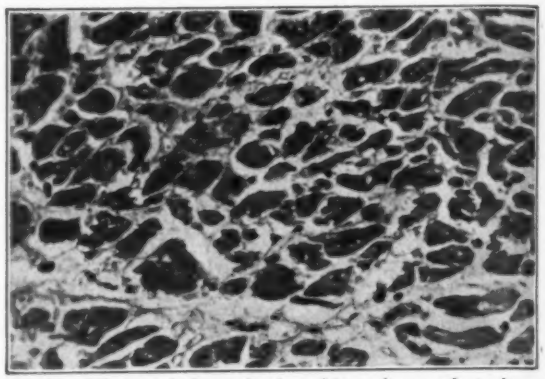


FIG. 14.—Microscopical examination of heart from patient whose E.C.G. is shown in Fig. 13. (×554.)

The incidence of this condition in patients admitted to public hospitals with a diagnosis of cardiac infarction is lower than that found in the general population. For instance, apart from the series of 161 cases reported here, of 139 cases of heart attacks seen privately and thought clinically to be possibly or probably due to cardiac infarction, 115 showed frank evidence of cardiac infarction electrocardiographically with leads ABC, and 24 showed these minor changes of "ischaemia at rest." This feature, recognized at the necropsy referred to above performed in August, 1955, has been re-emphasized recently for the standard leads in relation to S–T depression. The polarity of the ABC leads, since point X is close to zero potential (Nahum, Mauro, Chernoff, and Sikand, 1951), probably accounts for the fact that the current of injury in the degenerated muscle, as with frank infarction, also produces segment elevation in the tracing. Frey (1938) and Oettel (1941) describe elevation of RST during acute coronary insufficiency without infarction at necropsy.

*(ii) Abnormal T-wave forms in cardiac infarction.*—The cove-shaped inverted T wave is commonly seen in cardiac infarction with ABC leads as with standard leads. In addition the cove-shaped upright T wave may also indicate cardiac infarction with leads ABC as with standard leads. Such a case is illustrated in the following. Patient 109 was admitted to hospital with a history of eight hours' duration of sudden severe chest pain passing to the neck and down both arms; he lost consciousness, and on recovery of consciousness was cold and clammy. The ascent of the T wave (Fig. 15) is faster than the descent, it is peaked, and the T wave reaches its maximum after about 50–55% only of the interval from the Q wave to the extreme end of the T wave. Also, it is noticed that the "take-off" is slightly elevated and round-shouldered. This E.C.G. was taken eight hours after the onset.

This type of tracing may be replaced by a more usual pattern later, and in fact five days later this patient's E.C.G. revealed an inverted T wave with well-marked Q wave formation.

*(iii) Electrocardiographic diagnosis of cardiac infarction associated with heart block.*—The diagnosis of cardiac

infarction in the presence of heart block is regarded as a difficult one electrocardiographically. If an earlier tracing free of heart block is available and the E.C.G., taken immediately after symptoms and signs of cardiac infarction appear, shows heart block, this development is generally regarded as due to infarction. Such a case has already been reported with leads ABC (Trethewie, 1953). Right bundle block does not present such difficulty usually, though

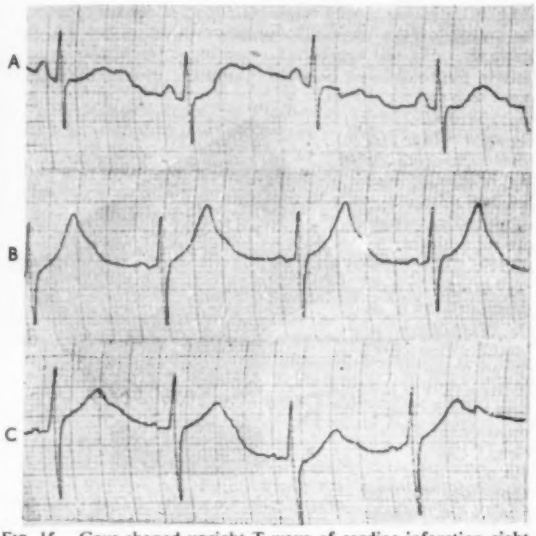



FIG. 15.—Cove-shaped upright T wave of cardiac infarction eight hours after onset.

it may be congenital. It was pointed out (Trethewie, 1953) that segment elevation is also evident in such tracings, while in block due to old fibrosis and electrolyte imbalance such segment elevation presents different features. Recently vector-cardiographic work has indicated a feature suggesting infarction associated with block, and this probably depends on the same feature fundamentally. In the present series 17 patients showed varying degrees of block.

There were five cases of left branch bundle block in this series. Three conformed to the pattern seen in hypertension with the gradual production of block following a left strain pattern. In one of these there was no notching of the S wave (first downward complex), but some slurring in leads A and B. In one, notching was present in this complex in A and C, and in one notching in A, B, and C. The B.P. in the first patient was 170/110 on admission. The sedimentation rose and there was a leucocytosis. The history was clinically significant of infarction, and the patient survived.

For comparison the findings in a patient who had no history suggestive of cardiac infarction, but who developed left bundle block associated with aortic regurgitation, are described. The tracing showed slurring only in lead A and not in lead B or C. This patient died two years later, and was shown at necropsy to have aortic incompetence, left ventricular hypertrophy, and some slight general fibrosis without evidence of infarction. Intensive microscopical examination of sections of the heart muscle failed to reveal any evidence of infarction or of sufficiently discrete fibrosis that might have suggested old infarction.

In the other two cases gross notching was present in A. In one the block pattern was also manifest in B and C with gross notching; but in the other leads B and C did not show such a broad biphasic swing pattern. These two, by their elevated segments, clearly indicated infarction. Segment elevation was of the CBa type in one (Patient 36), and the pre-necropsy diagnosis was "infarction: septal, antero-lateral, and slightly on the posterior surface." The standard E.C.G. showed left branch bundle block, which was thought, in view of the history, to be due to infarction but not conclusive of itself. The patient died 13 days after admission, and the infarct was found to be extensive and in the zones described. In the other (Patient 52) the left branch bundle block was described as atypical, leads B and C not showing the big biphasic swing, and the E.C.G. diagnosis was "antero-lateral infarction: B type, with old posterior infarction." At necropsy, six days later, a yellow gelatinous lamina of infarction was present in the anterior wall of the left ventricle towards the apex. A thrombus was present in the anterior descending branch of the left coronary artery a little below its origin, and there was also another complete occlusion of a small branch of the anterior descending branch. Further details of the distinction between block due to infarction and block due to other causes will form the substance of a separate paper.

Right bundle block patterns were seen in eight instances. Five conformed to a classical infarct pattern (Fig. 16) (Patient 29). This report read: "Old infarct (B) and recent infarct (C): recent septal infarction extending posteriorly with old infarction." At necropsy, 11 days later, "the left ventricle showed extensive recent infarction from the apex into the posterior wall of the left ventricle and anteriorly into the interventricular septum. Between the upper limits of this infarct and the AV junction there was evidence of older infarction." Fig. 17 shows the standard lead findings for this subject. The remaining three patients showed a more marked biphasic swing in the tracings, but segment elevation was present in lead A suggestive of infarction. Two of the latter patients died, and a necropsy was carried out on one. This showed the presence of septal infarction encroaching on the posterior and also slightly on the anterior surface of the heart. Of the former five, four died within a fortnight of the attack. The other patient was discharged on September 14, 1955, and has not returned to hospital. In one, necropsy was not performed; in the other three, infarcts were found—respectively, in the apex of the left ventricle and septum (Patient 22) in the whole of the apex of the left ventricle extending to the base of the septum (Patient 19); and extensively in the posterior wall of the left ventricle and extending anteriorly into the interventricular septum (Patient 29).

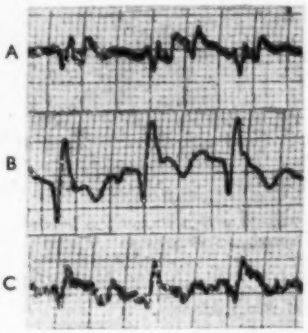



FIG. 16.—ABC-E.C.G. showing right bundle block due to cardiac infarction. Necropsy confirmation.

Two further patients showed intermittent right bundle block with classical signs of infarction in leads A and C.

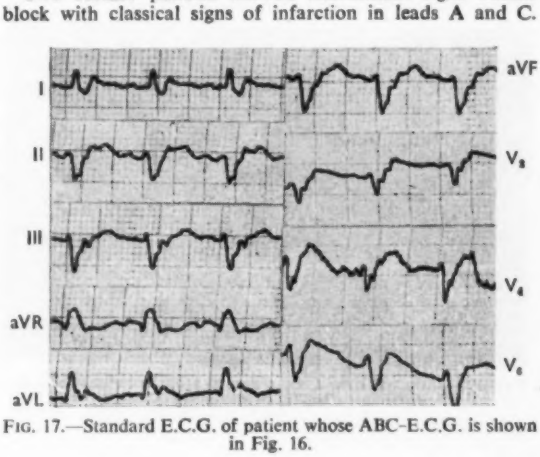



FIG. 17.—Standard E.C.G. of patient whose ABC-E.C.G. is shown in Fig. 16.

Both died, but necropsy was possible on only one, and extensive infarction was detected in the anterior part of the septum and the anterior surface of the left ventricle. In another patient (62) associated with acute ischaemia without actual infarction, the pattern in the standard leads appeared as partial bundle block, but in the ABC leads was associated with RSR' wave formation and slight segment elevation consistent with the diagnosis of acute ischaemia.

One patient showed Wenckebach's phenomenon, and one complete heart block. The former was recognized as posterior cardiac infarction with involvement of the septum. Also, in view of the upright Q in lead B (Trethewie, 1953),

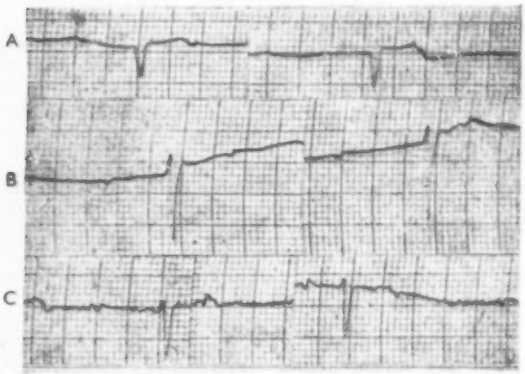



FIG. 18.—Wenckebach's phenomenon: varying PR interval with upright Q in lead B. Posterior cardiac infarction with septal patency. Further details in text.

it was suggested there might also be patency of the septum, but because of the varying block the timing of this wave was not so decisive (Fig. 18), although the T wave indicated that it occurred at the time of the Q wave. At necropsy posterior cardiac infarction was present, the septum was involved, and there was a patency in the infarct in the septum admitting the tip of one finger. The coronary arteries were perfused with radio-opaque material and a block was demonstrated in a large branch of the right coronary artery. The latter patient showed complete heart block, and the E.C.G. report (leads ABC) was "posterior cardiac infarction with involvement of the septum." Necropsy examination confirmed the presence and site of the infarct, and radio-opaque perfusion, carried out as before, showed a similar vascular occlusion.

### Theoretical Considerations (Standard Leads)

The action current produced by cardiac muscle as recorded by the intracellular electrode is largely a wide monophasic

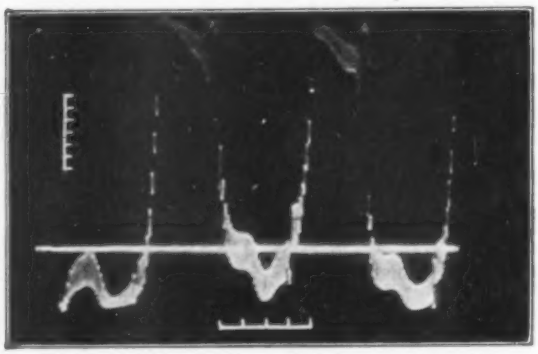


FIG. 19.—Intracellular E.C.G. obtained from beating toad heart. Potential: 5 mV. Time base: 0.2 sec.

potential pattern (Woodbury, Hecht, and Christopherson, 1951). We record such a pattern in Fig. 19, a tracing obtained from a toad heart. Kossmann (1954) pointed out that the E.C.G. as recorded in standard leads appears as an approximation of the first derivative $\left(\frac{dy}{dx}\right)$ of the intracellular action current curve. Nevertheless this should yield an inverted T wave, which occurs only in some leads. The phenomenon is probably due to the fact that excitation of the heart arises from the bundle tissue in an orderly fashion, the course of the bundle being downwards to the left and forwards. Fig. 20 represents recurring intracellular potentials in the toad heart (1, above), and the tracing (2, below) was obtained from lead C. The changed slope in the intracellular action current may be due to leakage of potassium from the microtip to the muscle fibre investigated, which develops slowly as the preparation remains, while early it conforms to the pattern of Fig. 19. Thus the S–T segment of the E.C.G. (lead C) is isoelectric, corresponding to the horizontal phase of the intracellular trace. Electrical fields are produced by the action currents, and points R (right chest at the base) and X (xiphisternum) develop potentials dependent partly on their distance from the source. The cardiac potentials decrease more rapidly, however, than theory suggests (Vanremoortere, 1956). Bipolar electrodes R, X (for example, lead C, 2, Fig. 20), simply record potential differences (dy) at their sites at any one instant; changes in successive instants of time (dx) then indicate Pot. $(R-X)=\frac{dy}{dx}$. This is an oversimplification owing to the multiplicity of heart motor units, but it does indicate the trend of the phenomenon. In the heart, multitudinous action currents are producing varying fields, which are manifest at any one instant by the recorded potential at that time, and there is a specific direction of spread as the successive motor units are excited. Recurring potentials are produced at various points throughout the body—for example, *$P_{(R)}$ at the right arm Einthoven terminal, $P_{(L)}$ at the left, and so on. The structure of the E.C.G. then forms a PQRST complex of approximately similar form from wherever it is recorded on the body surface from any two points, and even when recorded from the developing heart of the chicken. In certain instances the T wave is inverted, depending on the axis chosen for the leads.

FIG. 20.—Intracellular E.C.G.: (1) with corresponding lead C, (2) obtained from beating toad heart.

Einthoven ($E_1$) lead 1 then becomes $P_{(R)}-P_{(L)}$
($E_2$) lead 2 becomes $P_{(R)}-P_{(F)}$
($E_3$) lead 3 becomes $P_{(L)}-P_{(F)}$

Simple arithmetic yields, $E_1-E_2+E_3=P_{(R)}-P_{(L)}-P_{(R)}+P_{(F)}+P_{(L)}-P_{(F)}$
$=0$
$\therefore E_1+E_3=E_2$

Thus lead $E_2$ yields no further information than is already contained in $E_1$ and $E_3$, and is therefore redundant. Einthoven

*P refers to the potential change occurring throughout the cardiac cycle.

*et al.* (1913) reached this conclusion on different grounds. Likewise the Goldberger lead:

$$\text{aVR becomes} \frac{P_{(L)}+P_{(F)}}{2}-P_{(R)}$$

$$\text{and thus aVR} = -\frac{P_{(R)}-P_{(L)}}{2}-\frac{P_{(R)}-P_{(F)}}{2}$$

$$= -\frac{E_1}{2}-\frac{E_2}{2}$$

or aVR is the inversion of half the potentials of $E_1$, $E_2$, is derivable therefrom, and is therefore redundant. Similarly, aVL becomes $\frac{E_1}{2}-\frac{E_2}{2}$, and aVF becomes $\frac{E_2}{2}+\frac{E_2}{2}$; both therefore being derivable from the Einthoven leads, they cannot yield any more information than do the Einthoven leads. If capacitance is a factor of significance in relation to the points R, L, and F, which in itself is doubtful, the treatment is similar and becomes

$$\text{aVR} = -\frac{x}{x+y}E_1-\frac{y}{x+y}E_2$$

where $\frac{C_R}{C_L}=\frac{x}{y}$—that is, the relative capacity ($C_R$, $C_L$) of the points R to L is as x to y. The equation again shows that no further information can be obtained from the aV leads than is already derivable from the Einthoven leads. There is of course a further danger—namely, that segment depression in I and 2, say due to digitalis overdosage or electrolyte imbalance, becomes a segment elevation in aVR and might confuse unless care is taken in observing the type of contour of the elevation. The above treatment applies whether the body is regarded as an infinite homogeneous conductor or not, since we have defined points $P_R$, $P_L$, and $P_F$, as the actual potentials present. In point of fact the body is not an infinite homogeneous conductor, and the effect of surface restriction will be discussed later. This does not affect the correctness of the above treatment.

All of the above leads are in the frontal (anterior vertical) plane, which is largely defined by $E_1$ and $E_3$. In any case, no additional information can be supplied by $E_2$, aVR, aVL, or aVF, since they are concerned only with potentials at R, L, and F, as outlined, and can be derived simply from leads $E_1$ and $E_3$.

The Wilson terminal likewise yields potential changes $\frac{P_{(R)}+P_{(L)}+P_{(F)}}{3}$ and is not at infinity. $V_1$ becomes $P_{(V_1)}-\frac{P_{(R)}+P_{(L)}+P_{(F)}}{3}$, and similarly for $V_2$ to $V_6$. $V_4$, $V_5$, and $V_6$, then, record potentials almost solely in the frontal (anterior vertical) plane, $V_5$, precisely so, while $V_1$, $V_2$, and $V_3$ are only slightly askew to it.

One would therefore expect that $V_1$, $V_2$, and $V_3$, would more frequently produce evidence of infarction when $E_2$ and $E_3$ appear normal than would $V_4$, $V_5$, and $V_6$. Such is the case. On the other hand, possibly owing to the greater number of "normal"-appearing leads when only $V_5$ shows slight segment elevation (it is only slightly askew to the frontal plane) indicative of infarction and the remaining 11 leads appear normal, observers are hesitant to ascribe the due significance to changes in $V_5$ to which it is entitled. This feature was made more apparent in the earlier analysis. Furthermore, segment elevation of minor degree in $V_5$ may sometimes be regarded as indicative of a strain pattern when such is not the case. The "right-heart" V leads ($V_1$, $V_2$, $V_3$), when showing minor changes, are sometimes regarded by electrocardiographers as being of doubtful significance, probably largely because of this difficulty. The assessment of the ventricular gradient (Wilson, Johnston, Macleod, and Barker, 1934) is of value here.

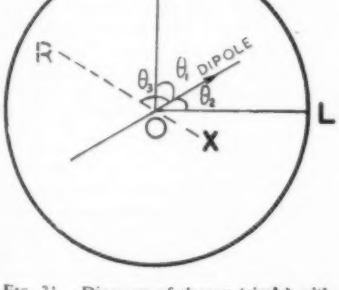



FIG. 21.—Diagram of thorax (circle) with heart at O indicated by a dipole. Further details in text.

## Theoretical Considerations* (ABC Display)

First let us consider the thorax in the simplified form of a conducting sphere with the heart (represented by a dipole with a direction) at the centre O of the conducting medium and then we shall modify the treatment as required for the conditions as they exist in the body (Fig. 21). Lead A is then represented as MX (M, manubrium; X, xiphisternum), lead B as LX (L, left axilla), and lead C as RX (R, right chest posteriorly), such that $\angle MXL=\angle LXR=\angle MXR=1Rt.\angle$. If the potential at $M=\phi_1$, at $L=\phi_2$, $R=\phi_3$, and at $X=\phi_4$, at any one instant, then we have

$$\phi_1-\phi_4=A \text{ (potential recorded by lead A)}$$
$$\phi_2-\phi_4=B \text{ ( \,,, \quad ,, \quad ,, \quad ,, B)}$$
$$\phi_3-\phi_4=C \text{ ( \,,, \quad ,, \quad ,, \quad ,, C)}$$

or $\phi_1-\phi_2=A-B$(?); $\phi_1-\phi_3=A-C$(?); $\phi_2-\phi_3=B-C$(?), all of which expressions are known, since A, B, and C are recorded precisely.

We shall consider the dipole as contained in a perfect conductor and the sphere also forming a surface conductor. Then successive changes in dipole strength will be associated with varying current flow. Now the potential $\phi$ at any point on the surface of a sphere

$$=\frac{3\,\mu\cos\theta}{a^3} \quad \ldots\ldots\ldots\ldots\ldots\ldots 1.$$

where $\mu$ = moment (strength) of dipole
$\theta = \angle$ of radius to direction of dipole
a = radius

and $\frac{\phi_1-\phi_2}{\phi_1-\phi_3}=\frac{A-B}{A-C}=\alpha$(say), which is known, since A, B, and C are known (recorded), also $\frac{\phi_1-\phi_2}{\phi_2-\phi_3}=\frac{A-B}{B-C}=\beta$ (say), which is known, then from (1) $\frac{\cos\theta_1-\cos\theta_2}{\cos\theta_1-\cos\theta_3}=\alpha$ (known) $\ldots\ldots\ldots\ldots 2.$

where $\theta_1$ is the $\angle$ subtended by M to the direction of the dipole
$\theta_2$ ,, ,, $\angle$ ,, ,, L ,, ,, ,, ,, ,, ,,
$\theta_3$ ,, ,, $\angle$ ,, ,, R ,, ,, ,, ,, ,, ,,

likewise $\frac{\cos\theta_1-\cos\theta_2}{\cos\theta_2-\cos\theta_3}=\beta$ (known) $\ldots\ldots\ldots\ldots 3.$

If we let the direction cosines of the heart "dipole" to any x, y, z right-angled axis system, be l, m, and n, and of axis of M, R, L be $l_1$, $m_1$, $n_1$; $l_2$, $m_2$, $n_2$; $l_3$, $m_3$, $n_3$; then, replacing in equation (3), we find

since $\cos\theta_1$ can be shown equal to $ll_1+mm_1+nn_1$
$\cos\theta_2$ ,, ,, ,, ,, ,, $ll_2+mm_2+nn_2$
$\cos\theta_3$ ,, ,, ,, ,, ,, $ll_3+mm_3+nn_3$

that $\frac{(ll_1+mm_1+nn_1)-(ll_3+mm_3+nn_3)}{(ll_1+mm_1+nn_1)-(ll_3+mm_3+nn_3)}=\alpha \quad \ldots\ldots\ldots\ldots 4.$

and likewise $\frac{(ll_1+mm_1+nn_1)-(ll_2+mm_2+nn_2)}{(ll_2+mm_2+nn_2)-(ll_3+mm_3+nn_3)}=\beta \quad \ldots\ldots 5.$

also it is known $l^2+m^2+n^2=1 \quad \ldots\ldots\ldots\ldots\ldots\ldots 6.$

$\therefore$ from (4), (5), and (6), l, m, n can be evaluated.
$\therefore$ we know the direction of the dipole from the recorded tracings ABC.

Thus we have determined the axis of the dipole.

Then if we let Q stand for $\frac{3\,\mu}{a^3}$

$$\text{from (1) then } Q=\frac{\phi_1-\phi_2}{\cos\theta_1-\cos\theta_2}$$

$$=\frac{\phi_2-\phi_3}{l(l_1-l_2)+m(m_1-m_2)+n(n_1-n_2)}$$

*This analysis was developed in collaboration with Mr. J. C. Taylor, Department of Mathematics, University of Melbourne.

Since we know $\phi_1$ $\phi_2$, see (p) above, and the denominator of the fraction contains terms we know, ∴ Q is known. Thus the moment (strength) of the dipole is known. Thus leads ABC define the dipole completely.

1. *Modification owing to the fact that the emanation is not precisely that of a dipole.*—Craib (1927) has presented strong evidence that we may regard the field as being produced by a dipole, and, since in the final analysis related ionic migration through muscle membrane is associated with the action current produced, this would appear to be a sound hypothesis. Let us first assume it is a point source at the centre producing an emanation of the type $f(t)$. The above treatment still holds, since we can select any particular instant in the cycle of $f(t)$ which will correspond to a selected dipole as treated above.

2. *The thorax is (a) not a sphere, (b) not a perfect conductor and impedance varies throughout its volume, and (c) the heart is not a point source at the centre.*—(*a*) If points M, L, and R ($\phi_1$, $\phi_2$, $\phi_3$) are not at equidistance from the centre and the thorax forms an ellipsoid since these variations are known, then the treatment is more complicated; but the actual conclusion—namely, that neither the strength (Q) nor the direction of the dipole (l, m, n) can be changed without producing a reflected change in lead A, B, or C—is a reasonable deduction. (*b*) This factor is difficult to evaluate. Kaufman and Johnston (1943) consider that variations of this nature, since they are not major, do not affect the recorded potentials greatly. (*c*) Though the heart is not a point source it is still theoretically possible to treat all the emanating points individually and summate algebraically, and therefore we should still obtain an equation related to the known findings appearing from leads A, B, and C. The final difficulty will arise if and when fields produced can annul one another as in precisely accurate phase difference of 180 degrees. This could not be expected to occur with infarction owing to the type of firing off of the heart muscle, and this has already been discussed.


## Summary

A series of 161 cases of cardiac infarction on whom ABC electrocardiograms were performed has been presented. Necropsies were done on 36 of these subjects.

The ABC display detected all cases of infarction detected by the present standard leads, and in addition detected infarction not demonstrated by them.

The correlation of infarct site with pattern changes in the ABC leads was determined theoretically and confirmed by necropsy studies.

E.C.G. patterns indicating cardiac degeneration short of discrete infarct formation, with one necropsy study, are described.

Abnormal T-wave form associated with infarction is illustrated.

Heart-block patterns associated with infarct formation are described and presented.

A theoretical analysis of the significance of the Einthoven, Goldberger, Wilson, and ABC leads is presented.


I thank the honorary staffs of the Royal Melbourne and St. Vincent's Hospitals for access to patients and Dr. Gerard Crock for the radio-opaque heart perfusions. I am indebted to Dr. J. D. Hicks, of the Royal Melbourne Hospital, and Dr. Tate Smith, of St. Vincent's Hospital, for access to and help in their departments of pathology.

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# INCIDENCE OF CORONARY ISCHAEMIA AFTER PARTIAL GASTRECTOMY


BY

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There are many studies relating coronary artery disease to various aspects of lipid metabolism. It has been shown that the incidence is high where the diet contains a large quantity of animal and saturated fat, and low where fat intake is poor (Keys, 1956). Following partial gastrectomy of the Polya type many patients lose weight and most are below their expected weight (Anderson *et al.*, 1955). This is probably due to a low calorie intake and post-gastrectomy symptoms, but impaired digestion and absorption of fat may be a contributory factor. Recent work in gastrectomy patients with $^{131}I$ labelled fats has shown increased fat excretion and diminished absorption after fatty meals and that fat loss is greater after the Polya operation than after the Billroth I (Everson, 1954; Shingleton *et al.*, 1957). This impaired fat absorption could be reflected in a lower incidence of coronary artery disease in gastrectomy patients.

## Material

Of 53 patients who had undergone the Polya type of partial gastrectomy 40 were traced and examined. All were males between 45 and 65 years who had been operated on for severe duodenal ulcer symptoms. The mean lapse of time from operation to interview was 9 years 10 months (range: 7 years 1 month to 13 years 4 months). At the same time, 40 men in the same age group with long-standing symptoms of duodenal ulcer (mean duration 17 years) were studied; 15 of these patients had suffered major complications such as perforation and haemorrhage. As a further control group we examined 40 "normal" males without ulcer or cardiac symptoms admitted for operative treatment of minor surgical and orthopaedic conditions (hernia, varicose veins, haemorrhoids, etc.). In the latter two groups the last five or six patients were selected on an age basis to ensure that the mean ages of each group were closely related (Table I).

## Methods

A clinical history and an examination of each patient were undertaken; height, weight, pulse rate, and blood pressure were recorded and a sample of venous blood was withdrawn for haemoglobin and lipoprotein estimations. Electrocardiography was performed, using a direct writer ("mingograph") before and after Master's (1950) double two-step test. The amount of exercise in this test is graduated according to the patient's weight and age. One man

with a previous myocardial infarction was not exercised, and in two others the exercise was discontinued because of angina; all others completed the test. To facilitate rapid recording after exercise only nine leads were used—the three standard leads and aVR, aVL, aVF, $V_2$, $V_4$, and $V_6$. The records were studied independently by two of us without reference to the patient's group, and the findings compared. A further independent opinion was obtained where a difference in interpretation occurred.

It is difficult to apply rigid standards to the interpretation of electrocardiograms, but the following criteria of ischaemia were adopted as a guide: ST depression of 1 mm. or more where the increase in pulse rate did not exceed 20 a minute and of 1.5 mm. or more where it did; flat or inverted T waves in appropriate leads; and multiple extrasystoles. All other abnormalities were noted and care was taken to distinguish changes due to tachycardia alone—namely a low RS-T junction with upward-sloping ST segment. The distinction between the lateral ischaemia of coronary artery disease and that of left ventricular strain is taken into account in the analysis of the results. A typical abnormal record is shown in Fig. 1. Fig. 2 shows alternate ventricular extrasystoles occurring after exercise. This, the only example of its kind, was accepted as evidence of ischaemia.

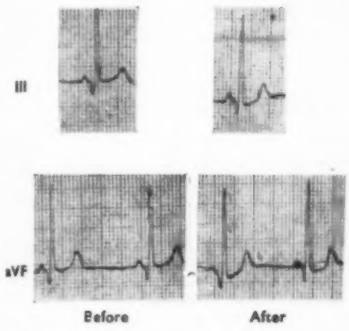


FIG. 1.—Posterior ischaemia after exercise.

The $\beta:\alpha$ lipoprotein ratio was estimated by standard methods of electrophoresis, Sudan-black staining, densitometry, and planimetry (Swahn, 1952). Pre-$\beta$ lipoprotein was noted when present (Besterman, 1957).

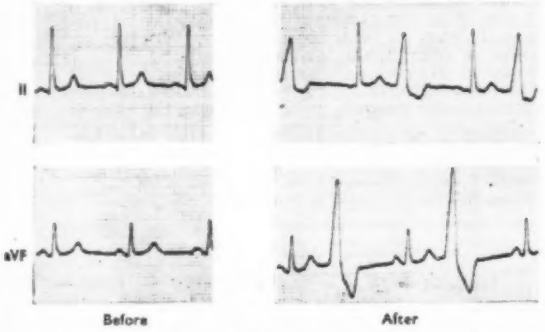


FIG. 2.—Alternate ventricular extrasystoles after exercise.

## Results

A summary of the principal findings is presented in Table I, and the abnormal electrocardiograms are classified in Table II.

The incidence of myocardial ischaemia in the gastrectomy group (six positive E.C.G.s) is less than in the control group (15 positives), and this difference is significant ($\chi^2 = 5.23$; $0.02 > P > 0.01$). The difference is even more significant when the gastrectomy group is compared with the ulcer group (21 positives) ($\chi^2 = 12.6$ and $P < 0.01$). The difference between the control and ulcer groups is not significant ($\chi^2 = 2.49$). If the electrocardiograms showing left ventricular (L.V.) strain are included in the analysis (Table II) the significance of the data is altered and the difference between the control and ulcer groups becomes less marked. The number of abnormals in each group becomes gastrectomy 7, control 18, and ulcer 21, so that for gastrectomy and control groups $\chi^2 = 7.05$ ($P < 0.01$) and for the gastrectomy and ulcer groups $\chi^2 = 10.80$ ($P < 0.01$).

TABLE I.—*Summary of the Principal Findings. Each Group Contains 40 Patients*

| Group | Mean Age (Yrs.) | Mean Hb % | Mean Weight | | No. of Ischaemic E.C.G.s | Mean $\beta:\alpha$ Ratio (Lipoproteins) | No. with pre-$\beta$ Lipoprotein |
|---|---|---|---|---|---|---|---|
| | | | lb. | kg. | | | |
| Polya gastrectomy | 53·2 | 88·2 | 132 | 59·9 | 6 | 2·17 | 16 |
| Range.. | 45–65 | 59–103 | 103–183 | 46·7–83 | | 1·12–4·00 | |
| Control .. | 53·6 | 96·7 | 154 | 69·9 | 15 | 2·42 | 17 |
| Range.. | 46–64 | 77–118 | 114–208 | 51·7–94·3 | | 1·17–4·24 | |
| Ulcer .. | 53·5 | 97·7 | 147 | 66·7 | 21 | 2·49 | 16 |
| Range.. | 47–64 | 80–112 | 110–202 | 49·9–91·6 | | 1·00–7·20 | |

TABLE II.—*Classification of the Diagnoses of the Abnormal E.C.G.s*

| | Post. Ischaemia | Post.-Lat. Ischaemia | Lat. Ischaemia | Ant.-Lat. Ischaemia | Ant. Ischaemia | Infarction | Extrasyst. | Total | L.V. Strain | Misc. |
|---|---|---|---|---|---|---|---|---|---|---|
| Polya gastrectomy | 4 | 1 | — | — | — | — | 1 | 6 | 1 | 1 Low voltage with emphysema |
| Control .. | 7 | 7 | — | — | 1 | — | — | 15 | 3 | 1 R.V. strain |
| Ulcer .. | 11 | 3 | 3 | 2 | 1 | 1 Healed post. infarct. | — | 21 | — | — |

These figures suggest that the cardiac status of the gastrectomy patient is better than that of his fellows. Because the gastrectomy group is much lighter than the other two (Table I) and the mean weight of the six ischaemic gastrectomy patients (154 lb.; 69.9 kg.) is greater than the group mean, it seems possible that ischaemia is related to weight. However, no correlation between absolute weight and ischaemia was found in the ulcer and control groups.

Each patient's expected weight, depending on height and age, was calculated from British tables (Levine, 1923), and Fig. 3 shows the deviation from expected weight in each group, with the corresponding distribution of ischaemic E.C.G.s. This demonstrates clearly that the occurrence of myocardial ischaemia is not prevented by being underweight, and that in this series ischaemia is not related to obesity, for 16 (38%) of the 42 ischaemic E.C.G.s occurred in subjects who were more than a stone (6.4 kg.) less than their expected weight; alternatively, 16 of 53 people (30%) whose weights were at least a stone (6.4 kg.) less than their expected weight had E.C.G. evidence of ischaemia. Thus while there is a clear difference in the weights of the groups, and while

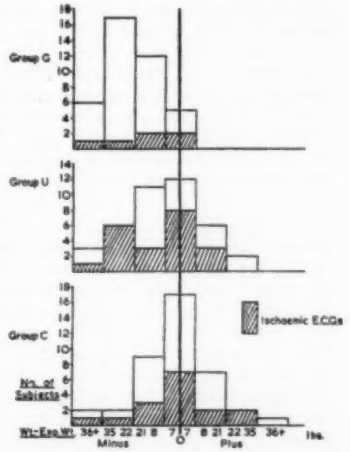


FIG. 3.—Distribution of ischaemic E.C.G.s and subjects' weights related to expected weights.

this corresponds to the incidence of myocardial ischaemia, weight by itself does not seem to be a specific factor.

There is a difference between the mean $\beta:\alpha$ lipoprotein ratios of each group (Table I). The ratio of the gastrectomy group is 89.5% of the mean control ratio and 87.0% of the mean ulcer ratio, but these differences are not significant ($P > 0.1$ in both cases). There is no difference between the mean ratios of the 42 ischaemic and 78 non-ischaemic patients, which are 2.38 and 2.35 respectively.

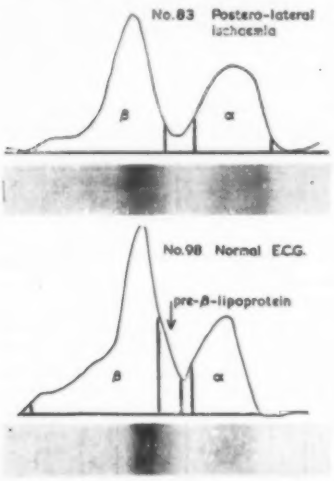


FIG. 4.—Normal lipoprotein pattern with abnormal E.C.G. (No. 83) and normal E.C.G. with pre-$\beta$ lipoprotein (No. 98).

Forty-nine patients in the series had a pre-$\beta$ lipoprotein band—19 (45%) of the 42 ischaemic patients and 30 (38%) of the 78 non-ischaemic patients. Fig. 4 shows the lipoprotein patterns in two people; one had ischaemia but shows no pre-$\beta$ lipoprotein band, the other had no ischaemia and does.

None of the other aspects investigated showed any significant difference between the groups, apart from the low mean haemoglobin level of the gastrectomy patients (88.2%). This is actually an adverse factor which would tend to increase the number of positive electrocardiograms in this group.

## Discussion

There is inevitably some selection of patients for gastrectomy. Nevertheless only one of the present ulcer group would be refused gastrectomy on a normal assessment of fitness, and all were fit 10 years ago. We consider that there is insufficient evidence of selection in favour of the gastrectomy group to invalidate the findings.

It may be argued that the incidence of abnormal electrocardiograms in this study is suspiciously high. Certainly Master *et al.* (1942) found no significant changes in the electrocardiogram following the double two-step test in 34 normal subjects of unspecified age. Against this, Riseman *et al.* (1940), employing criteria of abnormality more severe than Master's and comparable to our own, found significant changes in 10 of 15 normal patients whose ages ranged from 25 to 73 years. In a review of the literature they drew attention to the divergent findings of a number of authors. We cannot reconcile such differences. Here we are reporting results obtained from a standard test consistently applied to each of the clinical groups.

We believe that the cardiac status of the long-term gastrectomy patients is better than that of his "normal" or "ulcer" counterpart. Electrocardiographic evidence of myocardial ischaemia in the absence of anaemia is usually regarded as indicating coronary artery disease, and presumably the gastrectomy patients show less ischaemia because their coronary arteries are healthier. This suggests that in the time since operation their coronary vessels have either remained healthy and undergone minimal atheromatous change, or have even recovered from such change if initially present. In a pathological study Wilens (1947) concluded that regression of established atherosclerosis occurred in clinical states associated with severe short-term malnutrition and weight loss. This clinical study may support his view.

Weight loss by itself does not seem to be the main factor, and it is tempting to relate the lower incidence of ischaemia in gastrectomy patients to the diminished fat intake and impaired absorption which frequently occurs after a Polya gastrectomy. This, however, has not been reflected in a significantly lowered $\beta:\alpha$ lipoprotein ratio, nor can we demonstrate a relationship between pre-$\beta$ lipoprotein and myocardial ischaemia. It is true, however, that by the nature of Master's double two-step test we are dealing with coronary artery disease of less severity than that recently studied by Besterman (1957, 1958), and this may explain our inability to demonstrate the lipoprotein changes which he describes.

This study confirms the opinion of Douglas and Melrose (1955) that there is no increase in the incidence of coronary artery disease in ulcer patients compared with the normal individual.

## Summary

Evidence is presented which demonstrates a significantly lower incidence of coronary ischaemia in long-term gastrectomy patients compared with "ulcer" and "normal" controls.

This cannot definitely be related to lowering of the $\beta:\alpha$ lipoprotein ratio nor to changes in the pre-$\beta$ lipoprotein.

Although the gastrectomy patients are much lighter as a group there is no direct relationship between weight and ischaemia.

We thank Professor C. F. W. Illingworth for access to records and for the facilities so readily granted; Miss McCann for assistance with the electrocardiography; Miss Murray for secretarial help; and Mr. Kelly for preparation of the illustrations.

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"In these days it is not uncommon to hear in some quarters debates on the relative merits of science and the arts in education. In my own University College of North Staffordshire a regard for both these two branches of learning is considered essential in every undergraduate's studies, and we have, I think, achieved a very happy marriage between them. But it was long ago that Cambridge realized that both are equally important to a true university, and it emphasized its view by creating, in 1702, the Chair of Chemistry as one of the first dozen Chairs in the University. Since that time it has continuously expanded its activities and has established a tradition in natural science which is outstanding among the universities, not of this country alone, but of the world. What other university can match the names of Newton, Darwin, Clerk Maxwell, Thomson, Rutherford, and Hopkins—to mention but a few of its famous men?—H.R.H. PRINCESS MARGARET on the occasion of the opening of the new Chemical Laboratories at Cambridge on November 6 (*Cambridge University Reporter*, November 12).

# TEETH OF 5-YEAR-OLD LONDON SCHOOLCHILDREN (1957)

## WITH A COMPARISON OF THE RESULTS OBTAINED FROM 1929 TO 1957

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The first of a series of detailed surveys of the deciduous teeth of 5-year-old children was undertaken by one of us (M. M.) in 1929 at the request of the Board of Education. The children attended London County Council schools representative of the different parts of the Metropolitan area. Inspections at the same, or similar, schools have been made with colleagues at two-yearly intervals from 1943 to 1957, with the exception of 1953. In addition, children living in residential homes (institutions) and those attending private schools were visited in 1945 and 1950 for comparison with the London County Council children. (References to all these are given at the end of this report.)

The probe-and-mirror method of examination has been used throughout, and the criteria for structure and caries employed were those developed by Mellanby (1934). Both the method and the criteria have been described in detail in previous reports of this series.

When the surface of a tooth is smooth and shiny it is said to be hypoplasia-free—that is, the structure is good ($Hy_0$). Any roughness is graded according to type and degree, differentiation being made between the comparatively rare gloss hypoplasia (G-Hy) and the common M-hypoplasia (M-Hy) (King, 1940). The surface structure of the teeth is expressed both as the percentage incidence of the different grades of hypoplasia and as the average M-hypoplasia figure (A.H.F.). The latter gives a rough computation of the extent of this type of defect and is obtained by allotting a number to each tooth (1 for M-$Hy_1$, 2 for M-$Hy_2$, and 3 for M-$Hy_3$) and dividing the sum of these by the number of teeth. *Those showing gross hypoplasia and those so carious that assessment is impossible are excluded.*

A tooth is regarded as caries-free when no disease can be diagnosed by the method of examination employed. Caries is expressed as a percentage incidence—that is, d.e.f. per 100 teeth—and as the average caries figure (A.C.F.), which is estimated in a similar way to the A.H.F. The numbers 1, 2, and 3, are allotted to carious teeth according to the amount of tooth involved. Missing molars and canines are presumed to have been extracted for severe caries and are included in the $C_3$ group, while missing incisors (mainly lower centrals) are counted as having been naturally shed and are omitted from the analysis. The maximum value for both A.H.F. and A.C.F. is 3.

The Board of Education (1931) analysed the data obtained in the 1929 investigation, but published only the figures relating to *children* and not to individual teeth. A child was said to be caries-free who had no recorded decayed teeth, or only one, two, or three teeth with grade 1 caries, the second group being included because such a small proportion of the children were "caries-free." For the purpose of comparison the same classification has been perpetuated throughout these surveys, but, in addition, the results have been analysed for the incidence and extent of hypoplasia and caries in *each type of tooth.*

### Results

*Teeth Present.*—In 1957 the dental condition of 1,241 children were recorded. All of them had had their fifth but not their sixth birthday. At the time of the inspection there were 22,587 deciduous teeth *in situ* out of a possible 24,820 (91%). The percentage distribution of the individual types was similar to that in 1955 and in the earlier surveys (*Brit. med. J.*, 1957, **2**, 318)—namely:

| | Upper Jaw | Lower Jaw |
|---|---|---|
| Central incisors | 90.5 | 77.6 |
| Lateral ,, | 96.4 | 96.7 |
| Canines | 99.4 | 99.6 |
| 1st molars | 91.6 | 82.9 |
| 2nd ,, | 93.6 | 81.9 |

*Surface Structure.*—An examination was made of the surface structure of 98% of the teeth present in the mouth (see above) and the results for individual teeth compared with 1955 figures are given in Table I. All the teeth except the lower molars had a better structure in 1957 than in 1955. In both years the lower teeth had fewer defects than the upper. The best structure of all occurred in the lower incisors, in which 80.3% of the centrals and 64.1% of the laterals were non-hypoplastic, and the worst in the molars.

TABLE I.—*Surface Structure of Different Types of Teeth* (1957 *compared with* 1955)

| Type of Tooth | Total No. of Teeth Examined for Structure | | Percentage of Teeth | | | | | | | | Total Percentage of Teeth with M-Hypoplasia | | Percentage of Teeth with Gross Hypoplasia | | A.H.F.* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | $Hy_0$ | | M-$Hy_1$ | | M-$Hy_2$ | | M-$Hy_3$ | | | | | | | |
| | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 |
| Upper jaw: | | | | | | | | | | | | | | | | |
| Central incisors | 2,118 | 2,166 | 26·4 | 51·7 | 33·2 | 36·6 | 27·3 | 8·8 | 7·3 | 0·1 | 67·9 | 45·5 | 5·7 | 2·8 | 1·17 | 0·56 |
| Lateral ,, | 2,282 | 2,284 | 34·9 | 45·2 | 39·4 | 44·4 | 17·6 | 8·3 | 3·2 | 0·1 | 60·3 | 52·8 | 4·8 | 2·0 | 0·89 | 0·62 |
| Canines | 2,392 | 2,432 | 37·5 | 41·1 | 43·4 | 51·6 | 14·0 | 5·9 | 2·4 | 0·1 | 59·9 | 57·6 | 2·6 | 1·3 | 0·81 | 0·64 |
| 1st molars | 2,157 | 2,196 | 9·9 | 14·6 | 34·2 | 46·9 | 42·7 | 36·8 | 8·2 | 0·9 | 85·1 | 84·6 | 5·1 | 0·8 | 1·52 | 1·24 |
| 2nd ,, | 2,263 | 2,293 | 8·9 | 13·7 | 32·3 | 45·7 | 47·6 | 37·6 | 9·5 | 2·4 | 89·7 | 85·6 | 1·5 | 0·7 | 1·59 | 1·29 |
| Total upper jaw | 11,212 | 11,371 | 23·8 | 33·3 | 36·7 | 45·2 | 29·6 | 19·3 | 6·0 | 0·7 | 72·3 | 65·2 | 3·9 | 1·5 | 1·19 | 0·87 |
| Lower jaw: | | | | | | | | | | | | | | | | |
| Central incisors | 1,883 | 1,917 | 83·6 | 80·3 | 14·8 | 18·8 | 0·8 | 0·6 | 0·0 | 0·1 | 15·6 | 19·5 | 0·8 | 0·2 | 0·17 | 0·20 |
| Lateral ,, | 2,336 | 2,389 | 77·4 | 64·1 | 20·7 | 35·0 | 1·2 | 0·8 | 0·1 | 0·0 | 22·0 | 35·7 | 0·6 | 0·2 | 0·23 | 0·37 |
| Canines | 2,399 | 2,460 | 61·7 | 56·6 | 30·1 | 38·9 | 3·7 | 2·3 | 0·3 | 0·0 | 34·1 | 41·3 | 4·2 | 2·1 | 0·40 | 0·45 |
| 1st molars | 1,893 | 2,001 | 22·1 | 27·8 | 35·4 | 46·5 | 32·7 | 24·3 | 6·2 | 0·4 | 74·3 | 71·3 | 3·6 | 0·9 | 1·24 | 0·97 |
| 2nd ,, | 1,904 | 1,970 | 11·7 | 26·3 | 34·3 | 43·3 | 40·7 | 28·2 | 11·4 | 1·4 | 86·4 | 72·9 | 1·9 | 0·8 | 1·53 | 1·04 |
| Total lower jaw | 10,415 | 10,737 | 52·8 | 51·6 | 27·0 | 36·7 | 14·7 | 10·5 | 3·3 | 0·4 | 44·9 | 47·5 | 2·2 | 0·9 | 0·68 | 0·59 |
| Grand Total | 21,627 | 22,108 | 37·8 | 42·2 | 32·0 | 41·0 | 22·4 | 15·0 | 4·7 | 0·6 | 59·1 | 56·6 | 3·1 | 1·2 | 0·94 | 0·74 |

* A.H.F. = $\frac{\text{Total M-hypoplasia figure}}{\text{Total number of teeth examined for structure (excluding those with gross hypoplasia)}}$

TABLE II.—*Incidence and Extent of Caries in Different Types of Teeth* (1957 *compared with* 1955)

| Type of Tooth | Total No. of Teeth Assessed for Caries (inc. Extractions) | | Percentage of Teeth | | | | | | | | Total Percentage of Carious Teeth (d.e.f. per 100 Teeth) | | A.C.F.* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | $C_0$ | | $C_1$ | | $C_2$ | | $C_3$ | | | | | |
| | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 | 1955 | 1957 |
| Upper jaw: | | | | | | | | | | | | | | |
| Central incisors .. | 2,179 | 2,245 | 72·2 | 74·4 | 6·8 | 6·2 | 12·3 | 12·3 | 8·7 | 7·0 | 27·8 | 25·6 | 0·57 | 0·52 |
| Lateral ,, .. | 2,342 | 2,392 | 82·3 | 82·6 | 4·9 | 4·0 | 8·2 | 7·2 | 4·6 | 6·2 | 17·7 | 17·4 | 0·35 | 0·37 |
| Canines .. .. | 2,410 | 2,482 | 88·9 | 90·5 | 3·2 | 2·2 | 5·3 | 4·6 | 2·6 | 2·7 | 11·1 | 9·5 | 0·22 | 0·20 |
| 1st molars .. | 2,410 | 2,482 | 58·3 | 58·5 | 10·2 | 8·3 | 15·6 | 16·6 | 15·9 | 16·6 | 41·7 | 41·5 | 0·85 | 0·91 |
| 2nd ,, .. | 2,410 | 2,482 | 41·9 | 37·7 | 18·4 | 25·0 | 22·4 | 22·4 | 17·3 | 14·9 | 58·1 | 62·3 | 1·15 | 1·14 |
| Total upper jaw .. | 11,751 | 12,083 | 68·6 | 68·5 | 8·8 | 9·2 | 12·8 | 12·7 | 9·9 | 9·6 | 31·4 | 31·5 | 0·64 | 0·63 |
| Lower jaw: | | | | | | | | | | | | | | |
| Central incisors .. | 1,887 | 1,926 | 94·8 | 94·6 | 2·3 | 2·9 | 2·5 | 2·0 | 0·5 | 0·4 | 5·2 | 5·2 | 0·09 | 0·08 |
| Lateral ,, .. | 2,340 | 2,399 | 94·7 | 96·3 | 2·1 | 1·3 | 2·6 | 1·9 | 0·6 | 0·5 | 5·3 | 3·7 | 0·09 | 0·07 |
| Canines .. .. | 2,410 | 2,482 | 91·2 | 92·2 | 2·4 | 2·1 | 4·5 | 4·2 | 1·9 | 1·5 | 8·8 | 7·8 | 0·17 | 0·15 |
| 1st molars .. | 2,410 | 2,482 | 37·5 | 37·8 | 7·3 | 6·8 | 24·5 | 26·5 | 30·7 | 28·9 | 62·5 | 62·2 | 1·48 | 1·47 |
| 2nd ,, .. | 2,410 | 2,482 | 29·8 | 28·2 | 16·3 | 19·9 | 19·3 | 20·1 | 34·5 | 31·7 | 70·2 | 71·8 | 1·59 | 1·55 |
| Total lower jaw .. | 11,457 | 11,771 | 68·3 | 68·5 | 6·3 | 6·8 | 11·1 | 11·4 | 14·3 | 13·3 | 31·7 | 31·5 | 0·71 | 0·69 |
| Grand Total .. | 23,208 | 23,854 | 68·4 | 68·5 | 7·5 | 8·0 | 12·0 | 12·1 | 12·1 | 11·4 | 31·6 | 31·5 | 0·68 | 0·66 |

* A.C.F. = $\frac{\text{Total caries figure}}{\text{Total number of teeth (including extractions)}}$

particularly the uppers, where only 14.6% of the first and 13.7% of the second were free from hypoplasia.

Very few teeth had any mottling, and when present it was very mild. Such teeth were graded for M- and G-hypoplasia in the usual way.

*Incidence and Extent of Caries.*—Table II compares the incidence and extent of caries for each type of tooth and for all types together in 1957 and 1955. The two series were in close agreement. The proportion of carious teeth and the average caries figures in both upper and lower jaws, separately and combined, was approximately 31% and 0.6%. The lower incisors had the least caries (5.2% in the centrals in both years and 3.7% in the laterals in 1957, as against 5.3% in 1955) and the lower second molars the most (71.8% and 70.2% respectively). The upper first molars had less caries than the other molars (20–30% less in 1957 as compared with 16–29% less in 1955).

TABLE III.—*Treatment of Caries* (1943 *to* 1957)

| Year | Total No. of Carious Teeth (including Extractions) | Treatment | | | Total Percentage of Carious Teeth Treated |
|---|---|---|---|---|---|
| | | % Extracted | % Silver Nitrate | % Filled | |
| 1943 | 10,886 | 15·7 | 6·7 | 2·7 | 25·0 |
| 1945 | 3,545 | 9·6 | 2·8 | 2·4 | 14·8 |
| 1947 | 6,245 | 13·6 | 2·4 | 4·4 | 22·4 |
| 1949 | 3,553 | 15·3 | 0·6 | 3·9 | 19·8 |
| 1951 | 7,412 | 13·0 | 0·1 | 6·1 | 19·2 |
| 1955 | 7,326 | 16·7 | 2·3 | 11·1 | 30·1 |
| 1957 | 7,510 | 17·0 | 0·6 | 10·7 | 28·3 |

The average number of carious teeth per child was 6.1% in both years, but if the "caries-free" children were excluded the figure dropped from 7.2% in 1955 to 6.9% in 1957. The percentage of children caries-free or nearly so was also similar—20.7 in 1957 and 21.2 in 1955—but the percentage of "caries-free" children was less in the last survey—namely, 11.9 compared with 15.5.

*Treatment of Caries.*—Table III shows that in 1957, as in 1955, rather less than one-third of the carious teeth had been treated, approximately 17% had been filled, and 11% extracted. Only 0.6% appeared to have been painted with silver nitrate in 1957 compared with 2.3% in 1955, which accounts for the slight difference in the total treated.

TABLE IV.—*Caries Related to Superficial Staining of Teeth* (1943 *to* 1957)

| Year | Percentage of Carious Teeth in Children with: | | |
|---|---|---|---|
| | No Stain | Black or Dark-brown Stain | Green Stain |
| 1943 | 30·1 | 19·3 | 33·4 |
| 1945 | 23·1 | 15·4 | 33·0 |
| 1947 | 19·8 | 12·4 | 26·0 |
| 1949 | 25·8 | 16·9 | 30·0 |
| 1951 | 25·5 | 14·4 | 33·6 |
| 1955 | 29·1 | 20·2 | 39·2 |
| 1957 | 32·0 | 22·0 | 31·2 |

*Caries and Superficial Staining of Teeth.*—In the recent examination as in 1955 (Table IV), the children with black or dark-brown stain on any tooth had a smaller percentage of caries (22%) than either the children with no stain (32.0%) or those with green stain (31.2%).

## Comments and Conclusions

It may be said, after reviewing these results, that the caries picture of the 5-year-old children in the London County Council schools has shown little or no change since 1955, whether considered per child or per tooth. But, as mentioned in previous reports, there have been many variations both in structure and in caries experience of this age group since the original 1929 investigation.

The proportion of teeth present at examination was, on the whole, similar in the seven inquiries from 1943 to 1957.

The structure of the individual teeth has varied from year to year. There was in general an improvement up to 1947, but, later, variations occurred for which we cannot

TABLE V.—*Structure—Caries Relationship* (1957)

| Grade of Structure | Incisors | | | Canines | | | Molars | | | All Teeth | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total Examined | % Carious | A.C.F. | Total Examined | % Carious | A.C.F. | Total Examined | % Carious | A.C.F. | Total Examined | % Carious | A.C.F. |
| $Hy_0$ .. .. | 5,223 | 6·9 | 0·12 | 2,392 | 4·1 | 0·08 | 1,712 | 39·3 | 0·71 | 9,327 | 12·1 | 0·22 |
| $M–Hy_1$ .. | 3,003 | 14·5 | 0·27 | 2,212 | 9·7 | 0·18 | 3,860 | 50·9 | 0·92 | 9,075 | 28·8 | 0·52 |
| $M–Hy_2$ .. | 408 | 37·5 | 0·72 | 200 | 16·5 | 0·30 | 2,711 | 61·5 | 1·17 | 3,319 | 55·8 | 1·06 |
| $M–Hy_3$ .. | 7 | 71·4 | 2·00 | 4 | 25·0 | 0·50 | 111 | 78·4 | 1·75 | 122 | 76·2 | 1·72 |
| G–Hy .. | 113 | 37·4 | 0·63 | 84 | 17·9 | 0·25 | 66 | 69·7 | 1·33 | 265 | 39·2 | 0·68 |

TABLE VI.—*Comparison of Caries in Upper and Lower Teeth (1943 to 1957)*

| Year | Percentage of Carious Teeth | | A.C.F. | |
|---|---|---|---|---|
| | Upper Jaw | Lower Jaw | Upper Jaw | Lower Jaw |
| 1943 | 33·2 | 26·9 | 0·69 | 0·62 |
| 1945 | 28·5 | 24·5 | 0·57 | 0·54 |
| 1947 | 21·0 | 19·5 | 0·41 | 0·44 |
| 1949 | 26·7 | 26·6 | 0·52 | 0·57 |
| 1951 | 26·9 | 28·2 | 0·51 | 0·60 |
| 1955 | 31·4 | 31·7 | 0·64 | 0·71 |
| 1957 | 31·5 | 31·5 | 0·63 | 0·66 |

account. The present position is similar to that of 1951 for all teeth combined, but there are differences between the types of teeth. As already mentioned, the structure is better in 1957 than in 1955.

The relationship between the external structure of a tooth and caries experience (Table V) was in general the same as in the comparable surveys made since 1943. For all types of teeth grouped together caries was present in only 12.1% of those with no recorded enamel defects ($Hy_0$), a higher figure than previously found, but with severe defects the disease was much more prevalent. For instance, caries was found in 76.2% of teeth with grade three M-hypoplasia ($M\text{-}Hy_3$) and in 39.2% of those with the gross forms of defect (G-Hy). These figures nevertheless support the conclusion drawn from earlier work that the better the structure of a tooth, as diagnosed by the method previously described, the less likely is it to become carious.

The incidence and extent of caries declined from 1943 to 1947 but rose after that date until 1955, since when there has been little or no change. A comparison of the carious teeth in the upper and lower jaws from 1943 to 1957 (Table VI) is of interest. In 1943 the upper jaw had 6.3% more carious teeth than the lower. The decrease in the incidence of the disease noted up to 1947 was less in the lower than in the upper jaws, and the difference between the two fell to 1.5%. The rise in the proportion of carious teeth subsequent to 1947 was greater in the lower jaw, and in 1951 the percentage of such teeth in the lower was 1.3% greater than those in the upper jaw. By 1955, and also in 1957, the percentage in the two jaws was the same—namely, 31. This change in distribution of the disease between the two jaws is analysed in Table VII, which shows that the trend is mainly due to a decrease in caries in the upper incisors associated with a larger increase in the lower molars compared with the upper.

The proportion of carious teeth filled has increased from approximately 2.5 to 11.0% since 1943, the rise being most marked in the last two examinations (Table III). Although the percentage of teeth extracted has varied to some extent from year to year, it was also greater in 1955 and 1957 than at any of the previous inspections.

In 1957 the children with black or dark-brown stain had a smaller percentage of carious teeth than the children with no stain or green stain, as in previous surveys. The children with green stain in 1957, however, had approximately the same percentage of diseased teeth as the children with no stain, while in the preceding surveys they had a larger percentage.

Some of the factors which contributed to the marked improvement of the caries picture between 1929 and 1947 and the subsequent deterioration in later years, have been discussed at length in the previous reports. No further evidence has been forthcoming to modify the tentative conclusions given there—namely, that the reduction in the disease was partly the result of more scientifically controlled nutrition of pregnant women and infants during the war and post-war period of rationing, when among other things the calcifying properties of the diet were increased. The subsequent freer choice of diet when cheaper foods, including cereals, were more easily obtainable, together with the reduction in the consumption of milk and cod-liver oil, could account for some of the deterioration from 1947 to 1955. The work of Holloway *et al.* (1958) suggests that some of the increase in the incidence of caries in recent years may be due to the rapid growth in popularity of iced lollies and similar confections. The fluorine in the water could not have been concerned in the changes noted in these reports, as it has remained low and constant throughout.

Our thanks are extended to many who have helped directly or indirectly with the investigations. We are particularly indebted to the London County Council and Dr. J. A. Scott for permission to carry out the survey, to the head teachers and their assistants for the trouble they took to make our visits to the schools such a pleasure, and to the Medical Research Council for financing the work. We would also like to acknowledge gratefully the assistance given by Misses I. Allen and B. Hafner in the tabulation of the data and to Dr. P. J. Holloway for his help and criticism during the preparation of the report.

TABLE VII.—*Distribution of Caries* (1953 *to* 1957)

| Year | Percentage of Carious Teeth | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Central Incisors | | Lateral Incisors | | Canines | | 1st Molars | | 2nd Molars | |
| | Upper Jaw | Lower Jaw | Upper Jaw | Lower Jaw | Upper Jaw | Lower Jaw | Upper Jaw | Lower Jaw | Upper Jaw | Lower Jaw |
| 1943 | 37·6 | 4·9 | 20·3 | 3·7 | 9·5 | 6·9 | 42·0 | 54·0 | 56·5 | 61·0 |
| 1945 | 29·5 | 1·7 | 14·9 | 2·1 | 7·5 | 5·9 | 38·9 | 48·6 | 51·4 | 58·8 |
| 1947 | 22·2 | 1·7 | 10·6 | 1·7 | 6·9 | 4·1 | 30·6 | 43·3 | 34·4 | 43·0 |
| 1949 | 30·1 | 3·3 | 14·5 | 2·6 | 9·1 | 5·5 | 35·7 | 54·0 | 44·2 | 61·3 |
| 1951 | 30·0 | 3·8 | 15·4 | 3·5 | 7·2 | 5·6 | 34·2 | 56·9 | 47·7 | 65·1 |
| 1955 | 27·8 | 5·2 | 17·7 | 5·3 | 11·1 | 8·8 | 41·7 | 62·5 | 58·1 | 70·2 |
| 1957 | 25·6 | 5·2 | 17·4 | 3·7 | 9·5 | 7·8 | 41·5 | 62·2 | 62·3 | 71·8 |

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"It seems to me certain that there should be no strife between science and religion, for the great Creator of living beings was also the Creator of the harsh and ruthless natural laws we call Darwinic evolution. . . . The question arises, does the Creator now content himself with allowing human beings to follow their own dictates as a self-governing colony provided they keep themselves within the natural laws which have been arranged for them; or does He occasionally intervene in an "unnatural" or "supernatural" way? That question I think cannot scientifically be answered. Hardly anything happens which cannot be explained by natural causes, but revelations occur which are sudden and surprising enough to suggest an "unnatural" or "supernatural" origin as if the Creator had Himself directly intervened in the course of a human life. Who would be bold enough absolutely to deny the possibility of such an intervention?"—F. Parkes Weber, *The Advent of Life: an Agnostic's Dream About the Creation* (H. K. Lewis, 1958).

# RADIOIODINE TRACER TESTS IN THE DIAGNOSIS OF HYPERTHYROIDISM

BY

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The use of radioiodine, $^{131}I$, has now an established place as an aid in the diagnosis of hyperthyroidism, but there is no agreement on which radioiodine test is best for this purpose. Many indices of thyroid function have been proposed which variously involve the measurement, either serial or at fixed times after the administration of the radioisotope, of its accumulation by the thyroid, excretion by the kidneys, and concentration in whole blood, blood plasma, and saliva.

Indices dependent on measurements of the radioiodine content in the thyroid or in blood are considered preferable to those dependent on urinary excretion because of the problems involved, particularly for out-patients, in urine collection over set periods of time.

Almost all of the radioiodine tests advanced in the literature will distinguish between the frankly thyrotoxic patient and the normal subject, but the real usefulness of a test must lie in its ability to aid the diagnosis in clinically borderline cases, and in its simplicity.

It is often difficult to assess the relative merits of particular proposed indices of thyroid function, as the clinical material varies so widely from one group of workers to another. However, most of the more promising radioiodine indices have been compared with each other, the B.M.R., and the biochemical determination of protein-bound iodine (P.B.I.) by the Royal Melbourne Hospital group (Clarke and Aujard, 1954; Madigan and King, 1954; Winikoff, 1954; Clarke, Sherriff, and Winikoff, 1955) and by others (Goodwin, Macgregor, Miller, and Wayne, 1951; Fryers, 1956; McConahey, Owen, and Keating, 1956).

From the studies in Melbourne it has been concluded that the best single index of thyroid function is the biochemical determination of P.B.I., which separates both the hyperthyroid and hypothyroid groups from the normal or euthyroid group with a high degree of accuracy. Between 90% and 95% of the patients in each group, including a large number of clinically borderline cases, have been correctly classified by this index.

The determination of P.B.I., however, is technically difficult on account of the very low levels of iodine to be measured, and demands the utmost care in keeping the laboratory and apparatus completely free from iodine contamination. For this reason it has been hoped that the use of radioiodine, which is readily detected by its beta and gamma emanations, would provide a simpler index of thyroid activity.

The best radioiodine indices in the Royal Melbourne Hospital studies referred to above have been shown to be the measurement of plasma protein-bound radioiodine 48 hours after administration of the tracer dose (48-hour P.B. $^{131}I$) and a measurement dependent on the early uptake of radioiodine by the thyroid.

The 48-hour P.B. $^{131}I$ index is the one proposed by Goodwin *et al.* (1951), who have shown that the rapid removal of the radioiodine as iodide from the plasma, and its early reappearance in hormonal form in hyperthyroid patients, can best be distinguished from the much slower process in euthyroid patients 48 hours after the administration of the tracer dose. It is a convenient index in that it does not require intravenous administration of the isotope, but it does necessitate the patient's attendance a second time, and, furthermore, since the measurement of the 24-hour percentage retention of radioiodine by the gland is considered useful in assessing the size of the therapeutic dose in those cases subsequently treated with radioiodine (Fairley, Holman, and King, 1956), patients often have to attend the hospital three days in succession, the first day for the administration of the tracer dose and early thyroid uptake measurements, the second day for a 24-hour percentage thyroidal retention measurement in case subsequent radioiodine therapy is prescribed, and the third day for a blood sample for the 48-hour P.B. $^{131}I$ determination.

Several early uptake tests have been suggested, and all appear reasonably reliable. The thyroid clearance test of Myant, Pochin, and Goldie (1949), however, is laborious in that it involves serial measurements over the gland and the measurement of radioiodine in the blood plasma; the uptake rate factor of Oddie, Meschan, and Wortham (1955) involves measurements of thyroidal radioiodine at 1, 4, and 24 hours; while the thigh/neck clearance test of Foote and Maclagan (1951) and the uptake rate factors of the earlier studies at the Royal Melbourne Hospital also depend on serial measurements.

Pochin (1950) was the first to observe that a simple but efficient test would be an early comparison of the counting rate over the neck with that over the thigh following the administration of a tracer dose of radioiodine, and Rundle, Seldon, and Indyk (1956) have also found such an index to be useful. In thyrotoxicosis the thyroid rapidly takes up radioiodine from the circulating plasma, so the early neck counts will become higher than normal and the thigh counts will become lower than normal, resulting in the neck/thigh ratio being greatly increased.

In the series of cases reported here the thyroidal uptake and the neck/thigh ratio have been determined two hours after oral administration of the tracer dose, the patient having had nothing to eat for the three hours before the test. The time interval of two hours was chosen because it was considered that by that time the amount of radioiodine secreted from the thyroid and the effect of variations in the absorption rates of radioiodide from the intestinal tract would be small.

The percentage content of radioiodine in the thyroid at 24 hours, which is used in many centres as an index of thyroid function, has not been found to have diagnostic significance in the Royal Melbourne Hospital Unit. In some patients the radioiodine content of the thyroid falls greatly between 2 hours and 24 hours, and the 24-hour measurement is considered useful as a measure of the degree of retention of radioiodine by the gland, which is taken into account when assessing

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the size of the therapeutic dose of radioiodine required. This measurement is here referred to as the 24-hour percentage thyroidal retention.

### Technique

Certain dietary factors, medications, and special radiographic procedures involving substances containing iodine are known to influence the thyroidal uptake and turnover of radioiodine. In order that the dietary influence shall be minimal a diet which avoids foods with a high iodine content, such as fish foods, is prescribed for one week before the test. With regard to medication, thiourylene derivatives and carbimazole are discontinued for a minimum period of two weeks, and iodine preparations and thyroid for at least four weeks prior to the tracer test.

A tracer dose of 20 $\mu$c of radioiodine ($^{131}$I), carrier-free, is administered orally, the patient having had nothing to eat for the previous three hours. Two hours after administration measurements are made of the radioiodine content of the neck and thigh, using paired G10Pb geiger counters as previously described (Clarke and Aujard, 1954).

Since the accumulation of iodine by tissues other than the thyroid and kidneys is relatively small, it has been assumed that the $^{131}$I content of the tissue of the neck, excluding the thyroid, is approximately equal to the $^{131}$I content of a similar volume of tissue of the thigh. The geometrical arrangements of the counters in the neck and thigh units are such that the response of the thigh counters to a distributed source of $^{131}$I (as in the thigh) is three times the response of the neck counters to a similar source, hence thyroid counting rate = neck counting rate − ⅓ thigh counting rate and the neck/thigh ratio, which is here taken to mean

$$\frac{^{131}\text{I content of the tissue of the neck including thryoid}}{^{131}\text{I content of a similar volume of tissue of the thigh}}$$

will be equal to $\dfrac{\text{Neck counting rate}}{\frac{1}{3}\text{ thigh counting rate}}$

In those cases where radioiodine therapy is a considered possibility similar measurements are made at 24 hours.

At 48 hours a blood sample is taken for the determination of P.B. $^{131}$I, which is expressed as a percentage of the dose per litre of plasma. The details of the method are given below. The limits for the two-hour uptake, the two-hour neck/thigh ratio, and the 48-hour P.B. $^{131}$I determined in this study are given in Table I. The same criteria have been adopted in the clinical assessment of thyrotoxicosis as have been previously described from this unit (Madigan and King, 1954).

### Determination of 48-hour P.B. $^{131}$I

Two-millilitre samples of plasma are used. The plasma proteins are precipitated by adding 6 ml. of 10% trichloracetic acid, after which the suspension is centrifuged and the supernatant liquid poured off. The precipitate is washed twice with 6 ml. of trichloracetic acid, centrifuged, and the supernatant poured off. To the precipitate is now added 0.5 ml. of 2N sodium carbonate and 0.1 ml. of "teepol" (a commercial wetting agent) and the mixture is agitated with a glass rod until all has dissolved. It is then transferred quantitatively to an aluminium pan, dried gently by means of an infra-red lamp, counted by means of an EHM2 mica-window geiger counter, and compared with a standard radioiodine source.

### Results

This study covers all the patients who were referred to the radioiodine unit of the Royal Melbourne Hospital for investigation, and who were given subsequent radioiodine tracer tests during the 15-months period August, 1956, to November, 1957. Some of these were frankly thyrotoxic patients for whom tracer tests were required for the determination of the 24-hour percentage thyroidal retention of radioiodine used in the assessment of the radioiodine therapy dose, but these results are not considered in the final analysis.

Altogether, 156 consecutive tracer tests were carried out on 139 patients. Twelve tests on 12 patients have been excluded from the analysis, as it has not been possible to assign a final diagnosis in these cases. A further 44 tests have been excluded either because medication had not been discontinued for a sufficiently long period, or because the patient was considered to be frankly toxic.

The results of the remaining 100 tracer tests on 96 clinically borderline patients considered free from influencing medication are given in Table II. These 100 tests include 61 in which no known influencing medication had been given at all, 3 post-operative, 17 post-$^{131}$I therapy (minimum time interval since therapy being three months), and 19 others in which medication had been discontinued for longer than the prescribed period. In 52 tests the final classification was hyperthyroid and in 48 tests it was euthyroid. The final classification was decided after further observation and in some cases after a trial period of medication.

For various reasons not all the three radioiodine indices—that is, the two-hour uptake, the two-hour neck/thigh ratio,

TABLE I.—*Limits for the Three $^{131}$I Indices Presented*

| Classification | Two-Hour Thyroidal Uptake % | Two-Hour Neck/Thigh Ratio | 48-Hour P.B. $^{131}$I % Dose/Litre of Plasma |
|---|---|---|---|
| Hyperthyroid | ⩾55 | ⩾50 | ⩾0·5 |
| Indeterminate | >50–<55 | >35–<50 | >0·45–<0·5 |
| Euthyroid | ⩽50 (lower limit uncertain) | ⩽35 (lower limit uncertain) | 0–⩽0·45 |

TABLE II.—*Results of 100 $^{131}$I Tracer Tests on 96 Clinically Borderline Cases Considered Free from Influencing Medication*

| Final Diagnosis | No. of Tests | Two-Hour Thyroidal Uptake | | | 2-Hour Neck/Thigh Ratio | | | 48-Hour P.B. $^{131}$I | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Correctly Classified | Indeterminate | Incorrectly Classified | Correctly Classified | Indeterminate | Incorrectly Classified | Correctly Classified | Indeterminate | Incorrectly Classified |
| Hyperthyroid | 34 | 30 | — | 4 | 32 | 1 | 1 | 31 | 1 | 2 |
| Post $^{131}$I therapy | 10 | 9 | — | 1 | 9 | — | 1 | 10 | — | — |
| Euthyroid | 33 | 27 | — | 6 | 27 | — | 6 | 26 | — | 7 |
| Post $^{131}$I therapy | 2 | 1 | — | 1 | 1 | — | 1 | — | — | 2 |
| Hyperthyroid | 3 | 2 | — | 1 | 2 | — | 1 | | | |
| Post $^{131}$I therapy | 3 | 3 | — | — | 3 | — | — | | | |
| Euthyroid | 8 | 7 | — | 1 | 7 | — | 1 | | | |
| Post $^{131}$I therapy | 1 | — | — | 1 | — | — | 1 | | | |
| Hyperthyroid | 2 | 2 | — | — | | | | 2 | — | — |
| Euthyroid | 3 | 2 | 1 | — | | | | 3 | — | — |
| Post $^{131}$I therapy | 1 | 1 | — | — | | | | — | — | 1 |
| Totals | | | | | | | | | | |
| Hyperthyroid | 39 | 34 | — | 5 | 34 | 1 | 2 | 33 | 1 | 2 |
| Post $^{131}$I therapy | 13 | 12 | — | 1 | 12 | — | 1 | 10 | — | — |
| Euthyroid | 44 | 36 | 1 | 7 | 34 | — | 7 | 29 | — | 7 |
| Post $^{131}$I therapy | 4 | 2 | — | 2 | 1 | — | 2 | — | — | 3 |

and the 48-hour P.B. $^{131}I$—were determined in all cases, and Table II shows the subdivision of cases for which one or more indices were determined. These results have been grouped according to the final diagnosis and tabulated as correctly classified, indeterminate, or incorrectly classified for each index according to the limits given in Table I.

In addition, at the beginning of this study, the two-hour uptake and the two-hour neck/thigh ratio were determined in 20 tracer tests on 20 patients with no known thyroid abnormality, as a guide to the normal variation of these indices.

The 24-hour percentage thyroidal retention measurements made during the period of this study on patients and normal controls considered free from influencing medication are given in Table III.

TABLE III.—*24-Hour Percentage Thyroidal Retention Measurements for the $^{131}I$ Tracer Test on Patients and Normal Controls Considered Free From Influencing Medication*

| 24-Hour Retention Percentage | No. of Patients Classified as | | |
|---|---|---|---|
| | Hyperthyroid | Euthyroid | Normal Control |
| >90–100 | 2 | 3 | — |
| >80– 90 | 17 | 3 | — |
| >70– 80 | 24 | 4 | 2 |
| >60– 70 | 10 | 11 | 2 |
| >50– 60 | 7 | 5 | 3 |
| >40– 50 | 4 | 6 | 1 |
| >30– 40 | — | 1 | — |
| >20– 30 | — | 2 | 1 |
| >10– 20 | — | 1 | — |
| 0– 10 | — | — | — |
| | 64 | 36 | 9 |

## Discussion

In selecting the most suitable radioiodine tracer test for routine use, consideration has to be given to several factors —namely, the reliability and simplicity of the test itself, the demands on the hospital and hospital personnel, and the demands on the patient.

Bearing in mind that the patients studied here are clinically borderline cases, it can be claimed that classification by the two-hour uptake, the two-hour neck/thigh ratio, and the 48-hour P.B. $^{131}I$ is reasonably good. These tests require only oral administration of the radioiodine and there is no necessity to admit the patient to hospital.

For the 48-hour P.B. $^{131}I$ the patient has to attend hospital on two occasions, the first for the administration of the tracer dose, and the second for the withdrawal of the blood sample, both visits being short. However, the blood sample has to be processed and assayed, with consequent additional delay in obtaining the result.

For the two-hour uptake and the two-hour neck/thigh ratio the patient has to make only one visit to hospital, although this visit is perforce somewhat prolonged, but the result is known within minutes of the completion of the test.

The main purpose of radioiodine tracer tests, such as those described here, is to help the physician reach a diagnosis in those cases which do not present with clear-cut signs and symptoms, by yielding additional information concerning a particular aspect of thyroid function. To expect any test or index to group all cases accurately is unrealistic, since a wide range of thyroid activity in both normal and abnormal groups must be expected. To keep this point in mind it is felt that the results are best presented as in Table IV.

TABLE IV.—*Results of $^{131}I$ Tracer Tests on Borderline Cases Considered Free from Influencing Medication (to Nearest 5%)*

*48-Hour P.B. $^{131}I$*

80% of cases where result ⩾ 0·50% dose litre are hyperthyroid
95% " " " " ⩽ 0·45% " " euthyroid

*2-Hour Neck/Thigh Ratio*

85% of cases where result ⩾ 50 are hyperthyroid
90% " " " " ⩽ 35 " euthyroid

*2-Hour Thyroidal Uptake*

85% of cases where result ⩾ 55% are hyperthyroid
85% " " " " ⩽ 50% " euthyroid

The 24-hour percentage thyroidal retention measurements given in Table III and the uptake measurements generally are much higher than for many other centres, and another striking feature is the wide variation of results amongst the euthyroid and normal control groups. No explanation can be given for these observations, for no abnormal dietary factors are apparent in the community, and the dietary restrictions imposed for one week prior to the tracer test, as part of the test procedure, are very light and are considered unlikely to be the cause of the high values.

Some variation is to be found in index limits reported from various centres, and it is recommended that each centre should determine the limits applicable to its own conditions.

## Conclusion

The 48-hour P.B. $^{131}I$, the two-hour neck/thigh ratio, and the two-hour uptake indices, following oral administration of a tracer dose of radioiodine, are very useful aids in the diagnosis of hyperthyroidism in clinically borderline cases (Table IV). All three indices are reasonably easy to determine, but the two-hour neck/thigh ratio has the advantages that it does not depend on a measurement of the dose and would not be affected by the incomplete drinking of the dose.

The 24-hour percentage thyroidal retention of radioiodine has been found to have no diagnostic significance in Melbourne, but it is thought to be useful as a measure of the degree of retention of radioiodine by the gland, and is considered when assessing the size of the therapeutic dose of radioiodine required.

Measurements of the thyroidal uptake of iodine by euthyroid individuals in Melbourne are much higher than those reported from many other centres, although no abnormal dietary factors are apparent in the community.

## Summary

The two-hour thyroidal uptake, the two-hour neck/thigh ratio, and the 48-hour protein-bound radioiodine are useful indices in the diagnosis of hyperthyroidism. These indices can be determined after oral administration of the tracer dose of radioiodine, with minimal demands on the hospital staff and the patient.

The results of a series of 100 $^{131}I$ tracer tests on clinically borderline cases, subsequently classified as euthyroid or hyperthyroid, are presented in Table IV. This mode of presentation keeps the limitations of the tests obvious.

We are indebted to Miss E. V. Sherriff, of the Commonwealth *X*-ray and Radium Laboratory, who carried out the determinations of 48-hour P.B. $^{131}I$. Thanks are due to Mrs. J. Wall, of the Peter MacCallum Clinic, for assisting in many of the measurements, and to those members of the honorary medical staff of the Royal Melbourne Hospital who have referred patients for study.

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# AN ANABOLIC STUDY WITH NORETHANDROLONE IN FOUR ELDERLY UNDERWEIGHT MALES

BY

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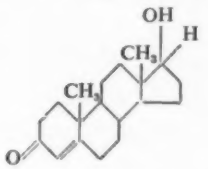
It has long been recognized that a substance which would bring about increased protein tissue synthesis in the body would be of considerable value to the clinician. The search for such a substance has been in progress for many years, and most of the work has been concerned with the steroid testosterone and its derivatives (Drill and Saunders, 1956). Testosterone, an androgen, was known to have powerful protein anabolic properties, but unfortunately the androgenic effects of this hormone regularly occur when the dose is sufficient to promote protein synthesis. This fact makes testosterone unsuitable as an anabolic agent except for very short periods of treatment. It seemed logical to make modifications of the testosterone molecule in an attempt to dissociate the androgenic from the anabolic property. Early experiments in this direction indicated that a significant degree of separation of the two activities of the androgens was possible.

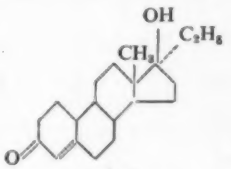
Amongst the modifications investigated were methyltestosterone, testosterone propionate, and a number of 19-nortestosterone compounds. The 19-nortestosterone compounds appear to be by far the most satisfactory, having a relatively low androgenic potency and yet retaining the high anabolic potency associated with testosterone itself (Hershberger *et al.*, 1953; Barnes *et al.*, 1954). A substance with a very high anabolic/androgenic ratio is the steroid norethandrolone (17$\alpha$-ethyl-19-nortestosterone). In animal studies it was shown to possess only about 6% of the androgenic potency of testosterone propionate although having a similar anabolic effect (Saunders *et al.*, 1957). Much work has been carried out with this substance, and it has been shown to be anabolic for both animals and man (Weston *et al.*, 1956; Saunders and Drill, 1956; Kory *et al.*, 1957; McSwiney and Prunty, 1957).

McSwiney and Prunty (1957) carried out an intensive study of the anabolic effects of norethandrolone and reported marked nitrogen retention and either an increase in body weight or a check in the fall of weight. They also observed a tendency to calcium retention; moreover, the phosphorus balance agreed with that calculated from nitrogen and calcium balance, which is considered to be evidence that the retained nitrogen is used in the formation of lean body tissue. According to Goodman and Gilman (1955), "the most familiar example of the anabolic effect of the androgens is the rapid growth and muscular development of the adolescent male. However, this anabolic action is also prominent in elderly and cachectic individuals. It probably provides a partial explanation of the symptomatic relief afforded by androgen therapy in certain debilitating diseases." This latter action is of particular interest since many elderly and undernourished patients fail to gain weight in hospital after treatment despite an adequate and well-balanced diet and absence of any active pathological lesion.

The object of this study was to investigate the anabolic effect of the steroid norethandrolone. Its structure and that of the parent steroid, testosterone, are as follows:



Testosterone



Norethandrolone

## Material and Methods

Four elderly men, age range 56–80, who were awaiting admission to Part III accommodation were chosen for this investigation because they had all recovered from the illnesses for which they had been admitted but had consistently failed to gain weight on an adequate diet of approximately 2,000 calories daily, containing 75 g. of protein. All were underweight for their height.

Before beginning the investigation they were examined to exclude the presence of any active disease, and it was confirmed that in each case the renal and liver function was not impaired. Serum bilirubin, alkaline phosphatase, thymol turbidity and flocculation, gold flocculation, and plasma protein estimations were used as indicators of liver function.

In order to estimate changes in metabolism brought about by treatment with norethandrolone, the following measurements were made: (1) naked body weight daily; (2) state of nitrogen balance throughout the study; (3) total body water or urea space and extracellular water or thiosulphate space before and after treatment.

*Body Weight.*—This was measured at the same time each day, the same scales being used throughout.

*Nitrogen Balance.*—All food and fluid taken during the study was recorded and the nitrogen content assessed from standard food tables. All urine was kept and analysed in three-day lots for its total nitrogen content by the micro-Kjeldahl method. The faecal nitrogen was assumed to be 1 g. daily in all cases.

*Total Body Water and Extracellular Water Volumes.*—The total body water was measured by the distribution of orally administered urea (McCance and Widdowson, 1951), and the extracellular water by the distribution of intravenously administered sodium thiosulphate (Cardozo and Edelman, 1952). All urea determinations were made with the Van Slyke manometric apparatus, and thiosulphate levels were determined potentiometrically with standard potassium iodate.

*Control Period.*—Each patient underwent a control period of from two to three weeks on an adequate diet providing 2,000 calories and 75 g. of protein daily. During this time a record was kept of the daily body weight. When the weight was constant and the patient was in nitrogen balance the measurements of total body water and extracellular water were made.

*Treatment Period.*—After successful measurement of the total body water and extracellular water the treatment period was begun. Two of the cases (J. R. and H. F.) were given 30 mg. of norethandrolone daily, but this dosage was subsequently increased to 50 mg. daily. The remaining two cases (H. C. and J. McK.) were given 50 mg. of the drug daily throughout the whole of the treatment period. The total

body water and extracellular water determinations were repeated when the gain in body weight appeared to have ceased.

## RESULTS

### Body Weight

As can be seen from Figs. 1 and 2, in all four cases there was a marked rise in body weight within a few days of the beginning of treatment. This increase in weight continued for a varying period of time—three days for H. F., nine days for J. R., and about 14 days for both H. C. and

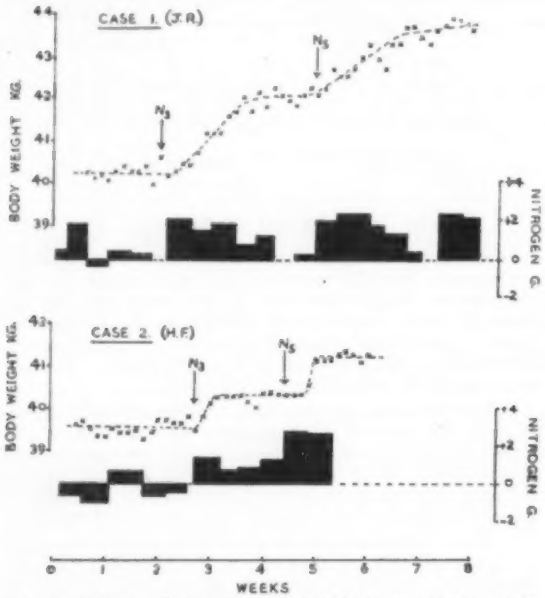



FIG. 1.—Diagram showing the relationship between body weight and nitrogen balance. Both cases began treatment with 30 mg. of norethandrolone daily (N3), but this was later increased to 50 mg. daily (N5).

J. McK. After this period of pronounced gain the body weight remained more or less constant. At this stage the daily dose of the drug was increased in patients J. R. and H. F. from 30 mg. to 50 mg. Within several days both patients showed a further increase in body weight, then again the body weight became more or less constant. The two patients (H. C. and J. McK.) who had 50 mg. of norethandrolone daily from the commencement of the treatment period appeared to gain weight more rapidly than did those who started with 30 mg. daily. In these patients, too, the body weight eventually reached a relatively steady state. Unfortunately, in the case of J. McK., measurements had to be interrupted owing to diarrhoea as a result of Sonne dysentery, and, although administration of the drug was continued, no body weights were recorded or urine collected until the infection was controlled.

The increases in weight, expressed as percentages of the body-weight levels during the control period, were 9% (J. R.), 4% (H. F.), 5% (H. C.), and 7% (J. McK.).

### Nitrogen Balance

The state of nitrogen balance is shown in Figs. 1 and 2. Nitrogen retention is depicted by the shaded area above the balance line and nitrogen loss by shading below the line. No urines were collected where the balance line is represented by a broken line.

During the control periods all four patients were considered to be in nitrogen balance, within the limits ±0.5 g. of nitrogen daily, but during treatment there was marked nitrogen retention in three of the cases. The fourth case (J. McK.) shows marked nitrogen retention until the onset of his diarrhoea, and finally a second nitrogen retention as he gained weight. As expected, in all cases the strongest nitrogen retention occurred where the body weight was increasing most rapidly.

### Total Body Water and Extracellular Water Measurements

*Total Body Water.*—As can be seen from the Table, all four cases showed an absolute increase in the total body water, although in the case of J. McK. this increase was not a significant one. The relative total body water—that is, total body water percentage of body weight—was increased in two cases (H. F. and H. C.); it was unchanged in the case of J. R. and decreased in J. McK.

*The Extracellular Water.*—The absolute extracellular water increased significantly in three of the four cases but was less for J. McK. The extracellular water percentage of body weight was increased slightly in two cases (J. R. and H. P.), unchanged in one (H. C.), and decreased in one (J. McK.).

### Side-Effects

The drug, which was administered orally three times a day in a total dosage of 30–50 mg., was well tolerated. No patients suffered from nausea or vomiting, nor were there any noticeable androgenic effects. An increase in appetite occurred during the treatment period, and the *non-protein* portion of the diet was increased slightly to cater for it. At the time of maximum gain in weight on the 50-mg. dose all patients were fully satisfied by the amount of food, and it was noted that occasionally some was refused, though all denied having nausea and none vomited. On this evidence it is doubtful whether a further increase in dose would have been well tolerated or desirable.

In the liver-function tests repeated after treatment there was no impairment of function.

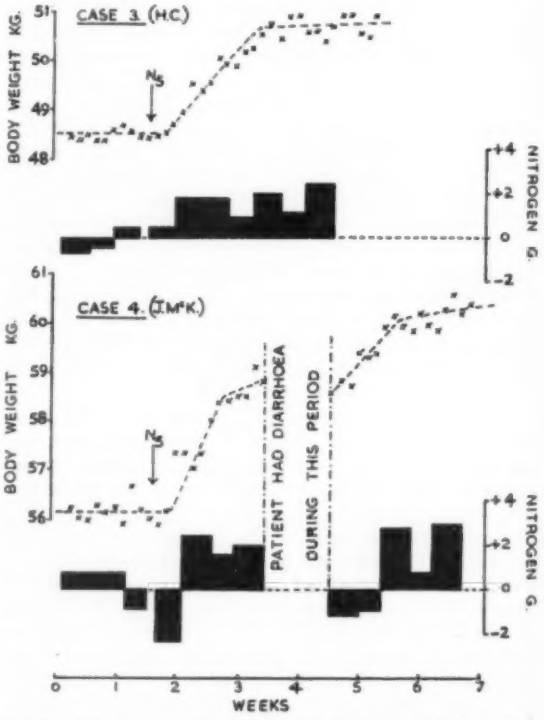



FIG. 2.—Diagram showing the relationship between body weight and nitrogen balance. Both cases had 50 mg. of norethandrolone (N5) throughout the treatment period.

*Comparison of Total Body Water, Extracellular Water, and Derived Intracellular Water Values Before and After Treatment with the Steroid Norethandrolone*

| Patient | Age | Surface Area (Sq. m.) | Time of Measurement | Body Weight (Kg.) | Total Body Water | | Extracellular Water | | Intracellular Water* | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Litres | % Body Wt. | Litres | % Body Wt. | Litres | % Body Wt. |
| J.R. | 68 | 1·43 | At end of control period | 40·2 | 28·9 | 72 | 9·4 | 23 | 19·5 | 48 |
| | | | After 42 days' treatment | 43·7 | 31·4 | 72 | 11·0 | 25 | 20·4 | 47 |
| | | | Difference | +3·5 | +2·5 | 0 | +1·6 | +2 | +0·9 | −1 |
| H.F. | 56 | 1·35 | At end of control period | 39·5 | 26·4 | 67 | 8·1 | 21 | 18·3 | 46 |
| | | | After 22 days' treatment | 41·2 | 28·5 | 69 | 8·9 | 22 | 19·6 | 48 |
| | | | Difference | +1·7 | +2·1 | +2 | +0·8 | +1 | +1·3 | +2 |
| H.C. | 80 | 1·60 | At end of control period | 48·4 | 32·8 | 68 | 11·1 | 23 | 21·7 | 45 |
| | | | After 25 days' treatment | 50·6 | 35·2 | 70 | 11·6 | 23 | 23·6 | 47 |
| | | | Difference | +2·2 | +2·4 | +2 | +0·5 | 0 | +1·9 | +2 |
| J.McK. | 77 | 1·56 | At end of control period | 56·0 | 29·9 | 53 | 13·5 | 24 | 16·4 | 29 |
| | | | After 28 days' treatment | 60·0 | 30·6 | 51 | 12·8 | 21 | 17·8 | 30 |
| | | | Difference | +4·0 | +0·7 | −2 | −0·7 | −3 | +1·4 | +1 |

* Intracellular water volume obtained from the difference of the total body water and the extracellular water volumes (i.e., T.B.W. − E.C.W. = I.C.W.).

## Discussion

The object of this study was to investigate the anabolic properties of the steroid norethandrolone in elderly underweight patients who consistently failed to gain weight on an adequate diet. From the results it would appear that this substance has definite anabolic properties. The four patients studied showed significant weight gain accompanied by marked nitrogen retention—two necessary requisites for the laying down of new lean body tissue. That this weight gain was in fact due to an increase in the lean body mass and not merely due to fluid retention should be more obvious after consideration of the total body water and extracellular water volumes before and after treatment.

Lean tissue gain is associated with an increase in both the absolute and the relative total body water values, and our results appear to follow this course. In all four cases there is an increase in the absolute total body water; there is an increase in the relative total body water in two of the cases (H. F. and H. C.), one is unchanged (J. R.), and the other (J. McK.) shows a slight decrease. The extracellular water values also support the view that the gain in body weight was lean body tissue and not merely fluid retention, since if the latter were the case we would expect large increases in the extracellular water. The increases which occurred, however, were not large, and in fact are compatible with the weight gain being totally accounted for as lean body tissue. The extracellular water percentage of body weight was increased slightly in two of the cases (J. R. and H. F.); it remained unchanged in one case (H. C.), and was slightly decreased in one (J. McK.). If the weight gain had been due to fluid retention we should have expected the extracellular water percentage of body weight to have increased by as much as 5 or 6% and not only 1 or 2% as we have found.

Fluid retention unaccompanied by an increase in the lean body mass would have had little effect, if any, on the absolute intracellular water volume. Our evaluation of the intracellular water volume—the difference between the total body water and extracellular water volumes—shows an absolute increase in the four cases studied. The intracellular water percentage of body weight is increased in three of the cases and decreased in one case (J. R.). It was unfortunate that J. McK. had acute diarrhoea during part of his treatment period, and this undoubtedly accounts for the decrease in the absolute and relative extracellular water values observed and also for the decrease in the relative total body water. Nevertheless, the increase in the intracellular water volume, together with the marked increase in body weight, shows that in this patient too an increase in the lean body mass occurred.

These results, together with the marked nitrogen retention, indicate that the gain in weight results from an increase in lean tissue and is not due to simple fluid retention. It appears, therefore, that the steroid norethandrolone is an effective protein tissue-building substance which is well tolerated and has little or no androgenic effects in these aged patients at a dosage of up to 50 mg. daily. According to McSwiney and Prunty (1957), 50 mg. of norethandrolone daily is as effective as 100 mg. Our investigation shows that 30 mg. does not produce the maximum anabolic response (Fig. 2), since a higher level of weight resulted from the administration of 50 mg. daily. The tendency to anorexia observed towards the end of the course suggests that a larger dose might cause nausea and vomiting in patients of the age group and sex investigated in this study.

We were not able to measure the body weight in the immediate post-treatment period, since the subjects were anxious to leave hospital after their prolonged stay, but the two we were able to follow (J. R. and H. C.) have maintained and subsequently increased their weight after seven months. McSwiney and Prunty (1957) reported that after cessation of treatment they have observed immediate nitrogen loss and quote a case in which nitrogen loss after withdrawal of the drug approximated to that previously gained. Kory *et al.* (1957), however, found that in a group of chronically underweight individuals 19 out of 25 subjects, followed for six months after the drug was discontinued, either maintained their weight or continued to gain. Our subjects and those of Kory were chronically underweight individuals, while those of McSwiney and Prunty were well nourished. This may explain the difference in findings. Where there is definite underweight or wasting the nitrogen retention due to treatment is perhaps permanent, but in a well-nourished subject the nitrogen retained may well be lost on withdrawing the drug.

## Summary

The anabolic effects of the steroid norethandrolone have been investigated in four elderly underweight patients.

In each case there was a significant gain in body weight associated with marked nitrogen retention.

Total body water and extracellular water measurements were made before and after treatment, and the results supported the view that the weight gain was due to an increase in the lean body mass and not merely due to a simple fluid retention.

No androgenic or other unpleasant effects were observed from use of the drug.

In our opinion norethandrolone has definite anabolic properties and should prove to be of considerable value for increasing the lean body mass in individuals who consistently fail to gain weight on an adequate diet.

Grants in aid of this study have been made to one of us (D. W.) by the Nuffield Foundation and by the Scientific and Research Subcommittee of the Newcastle Regional Hospital Board.

We wish to acknowledge the supply of norethandrolone ("nilevar") from Messrs. G. D. Searle and Co. Ltd.

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# ACTION OF METHALLENOESTRIL ON THE POST-MENOPAUSAL ENDOMETRIUM AND VAGINAL EPITHELIUM

## A COMPARATIVE STUDY

BY

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Methallenoestril ("vallestril") is a phenolic acid derived from naphthalene that has been shown to be more strongly oestrogenic than oestradiol when administered parenterally in oily solution to castrated female rats (Courrier, Horeau, and Jacques, 1947). It has the descriptive formula 3-(6-methoxy-2-naphthyl)-2,2-dimethylpentanoic acid. It is relatively insoluble in water and gastric contents, but soluble in alcohol, in oil, and in dilute bases such as occur in the intestinal secretions. Sturnick and Gargill (1952) have found methallenoestril to be effective in the control of "menopausal symptoms" and of the pain of post-menopausal osteoporosis, without causing uterine bleeding during treatment or after withdrawal.

Potency studies in the laboratories of the manufacturers have shown that, while the oestrogenic effect of methallenoestril on the vaginal epithelium of spayed mature rats is twice that of oestrone, its influence on uterine growth in immature mice is only one-tenth as potent as that of oestrone. The present investigation was undertaken to determine whether this selective oestrogenic action of methallenoestril was demonstrable in women, and this was done by comparing its action on the endometrium and vaginal epithelium with that of stilboestrol.

The subjects of the investigation were patients awaiting vaginal repair operations for genital prolapse in whom the menopause had occurred five or more years previously. Each of these was given a course of tablets labelled A, B, or C, the nature of which was unknown to the investigators until the study was complete. The course of tablets, one a day, was given for a period of between 40 and 84 days, and the interval between completion of the course and endometrial curettage at the time of the vaginal repair operation was between 4 and 15 days.

The tablets labelled A contained 5 mg. of methallenoestril, those labelled B were inert, and those labelled C contained 0.5 mg. of stilboestrol.

### Results

It may be seen from the Table that of the seven patients who received methallenoestril only one experienced withdrawal bleeding. This patient and one other were found to have hyperplastic endometrium. Of the 10 patients in the control group not one had withdrawal bleeding, although in three cases endometrial polypi were found, and in two of these the endometrium was relatively hyperplastic for a post-menopausal woman. Of the eight patients who received stilboestrol, four experienced withdrawal bleeding only, one induced bleeding, and one both induced and withdrawal bleeding. All of these, together with a seventh who did not bleed, were found to have hyperplastic endometrium. One patient had an endometrial polyp.

The diagnosis of "hyperplastic endometrium" was made on the basis of a naked-eye judgment of the amount and thickness of the endometrium confirmed by microscopical evidence of active proliferation or frank cystic hyperplasia. The four endometrial polypi (of which three occurred in the control group) were discrete adenomata arising by slender pedicles within the uterine cavity. They were considered to be innocent neoplasms rather than manifestations of hyperplasia.

The condition of the vagina was compared by noting the presence or otherwise of obvious atrophic changes in the epithelium. This was present in one of the seven methallenoestril cases, five of the 10 controls, and none of the eight stilboestrol cases.

Five patients volunteered the information that they felt better in general health and that their symptoms of prolapse were moderated after taking the tablets. Of these, three received methallenoestril and two the inert tablets.

*Tabulated Results*

| | Age | Years since Menopause | Days of Treatment | Interval before Curettage (Days) | Induced Bleeding | Withdrawal Bleeding | Atrophic Vaginitis | Endometrium: None or Scanty | Endometrium: Hyperplastic | Endometrium: Polyp |
|---|---|---|---|---|---|---|---|---|---|---|
| A. Methallenoestril | | | | | | | | | | |
| 2117 56 | 68 | 16 | 49 | 10 | – | – | – | – | + | – |
| 30661 54 | 65 | 15 | 63 | 15 | – | – | – | + | – | – |
| 46285 54 | 62 | 12 | 42 | 10 | – | – | + | + | – | – |
| 11174 56 | 62 | 10 | 42 | 10 | – | – | – | + | – | – |
| 13164 54 | 61 | 10 | 46 | 4 | – | – | – | + | – | – |
| 25128 55 | 58 | 10 | 62 | 10 | – | – | – | + | – | – |
| 10982 56 | 57 | 5 | 42 | 10 | – | + | – | – | + | – |
| B. Control | | | | | | | | | | |
| 26697 54 | 59 | 18 | 44 | 10 | – | – | – | + | – | – |
| 27838 52 | 56 | 14 | 41 | 10 | – | – | + | + | – | – |
| 11349 50 | 63 | 11 | 42 | 10 | – | – | + | + | – | – |
| 2800 49 | 57 | 8 | 43 | 10 | – | – | – | – | + | + |
| 21632 55 | 57 | 7 | 42 | 10 | – | – | – | – | – | + |
| 10316 55 | 59 | 5 | 44 | 8 | – | – | – | + | – | – |
| 392 57 | 55 | 7 | 63 | 10 | – | – | – | – | + | + |
| 5072 57 | 46 | 5 | 73 | 10 | – | – | + | + | – | – |
| 40193 56 | 59 | 10 | 84 | 10 | – | – | + | + | – | – |
| 27136 52 | 57 | 5 | 84 | 10 | – | – | + | + | – | – |
| C. Stilboestrol | | | | | | | | | | |
| 35248 53 | 59 | 19 | 40 | 10 | – | – | – | + | – | – |
| 925 49 | 57 | 9 | 44 | 8 | + | – | – | – | + | – |
| 373 56 | 57 | 7 | 41 | 10 | – | + | – | – | + | – |
| 4351 56 | 57 | 7 | 41 | 10 | – | + | – | – | + | – |
| 38570 56 | 66 | 14 | 69 | 10 | – | + | – | – | + | – |
| 23902 56 | 61 | 11 | 68 | 10 | – | – | – | – | + | – |
| 44359 49 | 61 | 8 | 63 | 13 | + | + | – | – | + | – |
| 18427 56 | 66 | 16 | 82 | 10 | – | + | – | – | + | – |

### Summary

A "double blind" trial of methallenoestril (vallestril) and stilboestrol has been carried out on 25 post-menopausal women awaiting vaginal repair operations.

Abnormal bleeding occurred in six out of eight patients who received stilboestrol and in only one of

the seven patients who received methallenoestril. Both macroscopic and microscopical examination of the endometrium has shown a lesser degree of oestrogenic stimulation in those who were given methallenoestril. The results may be largely explained by the fact that methallenoestril is a weaker oestrogen than stilboestrol, but there is some evidence of a selective action by the former which would make it a more suitable preparation for the treatment of post-menopausal vaginitis, post-menopausal osteoporosis, and the symptoms of the climacteric. A healthy vaginal epithelium was observed in all eight of the patients treated with stilboestrol, and all except one of the seven who were given methallenoestril. Five of the 10 controls had obvious atrophic changes.

We wish to thank Mr. Victor Lack, Mr. Alan Brews, and Mr. Robert Percival for permission to treat their patients and for their encouragement. The tablets for the investigation were prepared by G. D. Searle and Co.

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# A UNIQUE CASE OF AUTO-IMMUNE ERYTHROCYTE SENSITIZATION

BY

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Occasionally the red blood cells of an apparently normal person will be found to have a positive reaction when a direct anti-globulin test is carried out. Usually this can be demonstrated to be a "false positive" due to *in vitro* sensitization with the normal cold incomplete antibody. Very rarely is a true positive reaction found in healthy people (Dacie, 1950, 1954). Little has been written on this aspect of the antiglobulin test, and the occurrence in a blood donor of a true positive direct antiglobulin reaction must be very unusual.

Mr. X, group $A_1$, Rh genotype cde/cde, has given 26 donations of blood since 1941, and since 1948 has attended donor sessions regularly twice or three times each year. No trouble was experienced until his 25th donation in October, 1957. The hospital laboratory, selecting blood for one of their "dangerous" recipients, included an indirect antiglobulin test as well as saline and albumin techniques in the compatibility tests. Mr. X's blood was found to be "incompatible" by the indirect antiglobulin test, but compatible in saline and albumin media. As is the custom, this bottle of blood and the patient's serum were sent to us for investigation, when the donor's blood was found to give a moderately strong positive direct antiglobulin reaction, agglutinates appearing in about one minute. The patient's serum contained no antibodies. The apparent incompatibility on cross-matching was thus explained.

A direct antiglobulin test using serial dilutions of the reagent gave the results shown in Tables I and II. This gave the first surprise. The optimum reactions with Mr. X's cells were in the same range as the optimum for Rh (anti-D) sensitized cells suggesting a "warm" antibody was coating the cells. Inhibition of the reactions with γ-globulin showed the coating antibody was of the γ-globulin type—further confirmation that a "warm" type sensitizing antibody was involved. The second surprise came when a red-cell eluate prepared by Weiner's (1957) method was tested against a panel of cells of known phenotype and was found to contain the specific auto-antibody anti-$\bar{c}$. This was demonstrable by the indirect anti-globulin technique, but not in saline or albumin.

No abnormal antibodies were found in the serum. Tested against a panel of R.B.C.s, no abnormal agglutinins were present apart from a very weak auto- and pan-agglutinin demonstrable at 4° C. only. Neither cold nor warm haemolysins were detected. The Donath-Landsteiner reaction was negative.

The serological findings were those usually associated with a moderately severe haemolytic anaemia.

The haematological findings on January 25, 1958, were as follows: Hb, 92% (13.6 g./100 ml.); R.B.C., 4,510,000 c.mm); reticulocytes, less than 1%; W.B.C., 4,000 (polymorphs 52%, eosinophils 2%, lymphocytes 40%, monocytes, 6%). R.B.C.s and W.B.C.s apparently normal; platelets, 275,000. Hess test negative. Bleeding- and clotting-times normal. Prothrombin time normal. Red-cell saline fragility—within normal limits. No abnormalities were present, nor were any found on physical examination.

Past medical history included a hernia repair in 1939 and removal of a cartilage from a knee-joint in 1956. No history of any significant illness was given. Particular inquiry into any possible virus infection was made. He has never had a blood transfusion.

In March, 1958, a further donation was taken and the extensive serological tests were repeated. The direct antiglobulin reaction was still positive, and the pattern of the reaction was identical with that previously found. An eluate prepared from the red-cell stroma no longer had an anti-$\bar{c}$ specificity, having broadened its activity and now being, so-called, non-specific.

Dr. W. Weiner has completely confirmed the later serological findings and had some additional investigations done on the serum. Ultracentrifugal analysis gave perfectly normal results. A haptoglobulin estimation showed these to be definitely deficient, having a level only 50% of normal.

The fate of the man's blood donations since 1952 was investigated by inquiry of the hospitals using them. A particular point was made of asking whether any difficulty had been experienced in performing compatibility tests, particularly when the indirect anti-globulin technique had been used. The most recent occasion when the indirect antiglobulin test was used in a compatibility test was in November, 1955, and this was negative. Knowing that, using a single-dilution antiglobulin test, a positive reaction would have been obtained if present, there is no reason to doubt that in 1955 this donor's erythrocytes were normal. An antiglobulin test was not done on these cells again until the start of this investigation in November, 1957; the present state of autosensitization has therefore developed within the last two years.

TABLE I.—*Direct Antiglobulin Test*

| Final Dilutions of A.H.G. | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1,000 | 2,000 |
|---|---|---|---|---|---|---|---|---|---|---|
| Mr. X .. .. | w | w | w | (+) | + | ++ | ++ | ++ | + | + |
| Rh-positive cells, sensitized with anti-D .. | ++ | ++ | ++ | ++ | ++ | +++ | +++ | +++ | ++ | + |
| Rh-positive cells, unsensitized .. | + | w | – | – | – | – | – | – | – | – |

TABLE II.—*Direct Antiglobulin Test after Adding an Equal Volume of* 1/400 *γ-globulin to each Dilution of A.H.G.*

| Final Dilutions of A.H.G. | 4 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1,000 | 2,000 |
|---|---|---|---|---|---|---|---|---|---|---|
| Mr. X .. .. | – | – | – | – | – | – | – | – | – | – |
| Rh-positive cells, sensitized with anti-D .. .. | (+) | (+) | ? | – | – | – | – | – | – | – |
| Rh-positive cells, unsensitized .. | (+) | ? | – | – | – | – | – | – | – | – |

Mr. X is 44 years old and is a coal-miner working at the coal face. He has no complaints whatsoever. He has two abnormalities—a positive direct antiglobulin reaction and a low haptoglobulin level. An apparently healthy man with this type of true positive direct antiglobulin reaction and no significant previous illness seems to be unique.

This case obviously needs following before a final answer to the present finding can be given. The most likely explanation is that he has an acquired haemolytic "anaemia" which has been detected in a very early stage, and which is at present fully compensated, although one might have expected a higher reticulocyte count. The low haptoglobulins suggest that haemolysis may be active. Nosslin and Nyman (1958) found these levels to be low in haemolytic diseases. The serological findings are those of a haemolytic anaemia; the haematological findings are normal. The picture is very similar to that sometimes seen in known cases of acquired haemolytic anaemia, either during natural remission or after treatment with steroids or by splenectomy. It remains to be seen whether in the course of months or years the present findings will change and show the full picture of an acquired haemolytic anaemia.

A further examination of specimens taken in October, 1958, showed no change. The haemoglobin level was normal and the red cells still showed the same degree of sensitization.

Acknowledgments are due to Dr. W. Weiner for the great interest he has shown in this case, and to Dr. E. K. Blackburn for carrying out the haematological tests.

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# BILATERAL THROMBOPHLEBITIS AFTER A SINGLE DOSE OF ERGOTAMINE TARTRATE FOR MIGRAINE

BY

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Although ergotamine tartrate has such a well-established place in the treatment of the acute attack of migraine and the toxic effects of ergot and its alkaloids are so often quoted, the incidence of thrombophlebitis occurring after ergotamine tartrate has not often been recorded; in fact, only one reference has been found—that of Sir Russell Brain (1947), who, writing on the treatment of migraine, states: "Ergotamine tartrate has a highly specific effect on the headache . . . there seems no risk of ergotism, but pregnancy and arteriosclerosis are contraindications, and, rarely, a single dose may cause thrombophlebitis."

Below are given the case histories of three patients who in one practice in the course of two years have developed bilateral thrombophlebitis following a single dose of ergotamine tartrate.

## Case 1

A married woman aged 42, with two children, was diagnosed by an ophthalmic surgeon in 1954 as suffering from migraine, precipitated by strong sunlight. The wearing of dark glasses seemed to prevent the recurrence of any severe attacks, but ergotamine tartrate ("femergin") was prescribed in case of need.

On May 11, 1955, she developed an acute attack of migraine and took her first dose of ergotamine (two 1-mg. tablets) at 11 a.m. About 2 p.m. the headache disappeared quite suddenly, but she experienced a cramp-like pain in her right calf. This pain persisted and grew in severity throughout the afternoon and evening. In the night she was very restless with the pain and began to have sharp pains in the left leg. In the early hours of the following morning she was unable to stand up.

Examination later that morning showed that she was afebrile and had no gross varicose veins; but a dull red line, which was very tender, was present over the course of the long saphenous veins in the right leg, extending about a quarter of the way up the right thigh. A similar red line, also very tender, was present in the left leg, but this did not extend above the knee.

Both legs were strapped with "elastoplast," sorbo-rubber strips covering the affected veins, and she was encouraged to be ambulant. Within 24 hours she was much easier, all symptoms had gone within four days, and when the strapping was removed after 12 days there was no evidence of any residual thrombosis. She did show some varicosity of the long saphenous veins, more marked in the right leg.

## Case 2

The patient, a married man aged 44, had a history of marked varicose veins in both legs, for which he had had injections in 1942, which had been followed by a troublesome phlebitis. This had dissuaded him from any surgical procedure, and he had resigned himself to a below-knee elastic support. He had also managed to change from a manual occupation to a sedentary job in May, 1956—a change which had relieved his leg symptoms but aggravated his migraine.

On July 19, 1956, he received his first prescription for ergotamine tartrate, and on July 23 he had a typical migraine attack on rising. He took two 1-mg. tablets sublingually about 9 a.m. (it was Sunday) and then had a little breakfast. His headache began to ease and he decided to seek some fresh air in the garden. About 10.30 a.m. he was compelled to return indoors with severe pains in both legs. The pains increased, and by lunch-time he was only capable of lying on his bed. After a restless day and night he found numerous red lines on both legs.

Examination then revealed an intensive network of very tender red lines over both legs and extending half-way up each thigh. He was admitted to hospital, and the following day both long saphenous veins were ligated at the saphenous opening to obviate the danger of pulmonary emboli. He made a steady recovery.

## Case 3

A married man, a shop-proprietor aged 44, whose mother had suffered from asthma, was first diagnosed as suffering from migraine in 1952. Codeine tablets usually relieved the attacks, but in February, 1957, they became more frequent and he was subsequently kept on a modified Gowers mixture as a preventive. On March 23 he had his first prescription for ergotamine in the form of "cafergot."

On April 5 he felt a typical attack starting on rising. He returned to bed and swallowed his first dose of ergotamine tartrate (two tablets) at 10.30 a.m. He fell asleep, and awoke at 2 p.m. with his headache gone but having severe pains in the varicose veins in both calves. He remained in bed, and slept through the early part of the night, but found himself unable to stand the next morning owing to severe pains in both legs, the left being the worse.

Examination revealed a tender red line over a vein in his left leg, extending for about 4 in. (10 cm.). He had a small area of tenderness over a vein in the right calf but no redness. Both legs were strapped with elastoplast; he was much better in 48 hours, and when the strapping was removed after one week no signs of thrombosis or phlebitis were present.

### Discussion

Von Storch (1938), in a review of an early trial of ergotamine tartrate for migraine, mentions perivascular pains and pains in varicose veins as a rare complication. Spasm of the saphenous vein is referred to by Clarke (1957). The observation of Russell Brain quoted above is, however, the only reference to thrombophlebitis occurring after ergotamine; he mentions it as happening after a single dose, which is confirmed by the above three cases.

The third case is particularly interesting, for the difference between this patient's two legs tends to suggest that the pain which occurs in varicose veins following ergotamine may be the first stage of a thrombophlebitis.

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## SALT INTAKE AND HYPERTENSION

BY

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Hypertension was found by Dahl and Love (1957) to be associated with a high dietary intake of salt. In a group of 1,346 adults, habits of salt intake were classified as follows: (1) low intake—never add salt to the food at table; (2) average intake—add salt to food after tasting if insufficiently salty; and (3) high intake—routinely add salt to foods customarily salted before tasting.

TABLE I.—*Correlation of Salt Intake and Hypertension in* 1,346 *Adults*

| | No. in Group | No. with Hypertension |
|---|---|---|
| Low intake | 135 | 1 |
| Average intake | 630 | 43 |
| High intake | 581 | 61 |

Hypertension was significantly more frequent among those with a high intake than among the average group (Table I, $p<0.01$).

Dahl (1957) also studied the sodium excretion in hypertension, assuming that sodium is the important ion and that sodium excretion normally reflects intake with reasonable accuracy. The average sodium excretion of nine hypertensive men was $204.3 \pm 27.3$ mEq/24 hours, while the average excretion of 19 men with normal blood pressure was $165.7 \pm 32.0$ mEq/24 hours. The difference is significant ($p<0.01$). In the present work sodium excretion has been measured in a larger group of men with hypertension.

### Method and Results

The 24-hour urinary excretion of sodium has been measured in 20 men with hypertension and in 20 men with normal blood pressures. Blood-pressure levels over 140/90 mm. Hg have been regarded as abnormal. The mean age of the group with hypertension was 49.8 years, and their mean blood-pressure level 218.9/127.3 mm. Hg. The mean age of the normotensive group was 56.3 years. All were out-patients, taking their normal home diet and unaware that their salt intake was being investigated. The work has been confined to men because of the greater difficulty of collecting samples in women and because of premenstrual sodium retention. Sodium was estimated by flame photometry.

The mean sodium excretion of the 20 men with hypertension was 156.3 mEq/day (S.D.=54.6). The mean excretion in the 20 with normal pressures was 154.1 mEq/day (S.D.=46.2). The difference is not significant.

In this small group little reliance can be placed on differences in the subjects' accounts of their dietary habits. It is of interest, however, that high salt intake was commoner among the men with normal blood pressures (Table II).

TABLE II.—*Salt Intake in* 20 *Men with Hypertension and* 20 *Men with Normal Blood Pressures*

| | Salt Intake | | |
|---|---|---|---|
| | High | Moderate | Low |
| Normal blood pressure | 9 | 10 | 1 |
| Hypertension | 4 | 15 | 1 |

### Discussion

The present results do not confirm the findings of Dahl and Love (1957) that hypertension is associated with a high sodium intake and excretion.

There is other evidence suggesting that sodium plays an important part in the pathogenesis of hypertension. Hypertension is extremely rare among the Australian aborigines (Hicks and Matters, 1933), the Cuna Indians of Panama (Kean, 1944), and the tribes from the Szechwan mountains of West China (Morse and Beh, 1937). A factor common to all these peoples is a low sodium intake of 1–2 g. or less a day, but many other factors, nutritional or genetic, may be responsible.

With restriction of dietary salt to less than 250 mg. a day, the blood pressure falls in most hypertensive patients and rises again if more salt is added (Kempner, 1948). Moreover, Perera and Blood (1947) found that the rise in blood pressure of hypertensive subjects resulting from deoxycortone could be prevented by restriction of sodium intake. They showed also that an increase of dietary sodium chloride from 4 to 15 g. daily produced a slight but definite rise in blood pressure in six patients with hypertension.

In rats the use of 2% sodium chloride as drinking-fluid for six weeks produces hypertension and renal hypertrophy (Sapirstein *et al.*, 1950). The feeding of salt also enhances the hypertension resulting from experimental renal ischaemia (Verney and Vogt, 1938), and salt restriction prevents production of hypertension in rats by deoxycortone injection (Braun-Menendez, 1951).

### Summary and Conclusions

The sodium excretions of 20 men with hypertension and 20 men with normal blood pressures did not differ significantly. Other evidence suggests that sodium is necessary for the production of hypertension. In our society, however, hypertension cannot be related simply to dietary sodium intake.

I thank Dr. George Discombe for the sodium estimations. This investigation formed part of work awarded the Central Middlesex Hospital Research Prize for 1958.

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# Medical Memorandum

## A Simple Procedure for Early Detection of Hypofibrinogenaemia

For the diagnosis of hypofibrinogenaemia or afibrinogenaemia the Kjeldahl or simpler "fibrindex" (Ortho) method is most frequently used. Weiner *et al.* (1953) suggested a "bedside" method, the so-called "clot-observation test." In cases suspected of afibrinogenaemia blood is withdrawn into a test-tube. If clotting has not occurred in 10 minutes, disturbance of the fibrinogen level can be assumed. One of us (G. L. B.) suggested the incorporation of this method in the admission routine, dispensing with the use of a test-tube. The following procedure has been used in our department for the past year:

In all cases of ante-partum haemorrhage the admitting house-surgeon takes off blood for cross-matching—a routine followed in most maternity units. He notes the time when taken and proceeds with the admission routine. Ten minutes later he observes the sample. If it has not clotted he considers the patient to be suffering from hypofibrinogenaemia. In cases where resuscitative action must be taken immediately—and it is in just such cases that a rapid diagnosis is needed—he can at once proceed and return to the sample later.

We believe hypofibrinogenaemia is not as rare as is usually suggested. Of the 2,176 cases admitted to the maternity unit of the North Middlesex Hospital during 1957, four had proved hypofibrinogenaemia or afibrinogenaemia (an incidence of 1 in 544), and two of these were diagnosed on admission by employing this simple test.

The first case was one of severe post-partum haemorrhage after a spontaneous unexplained stillbirth, where it was noted that the sample taken for cross-matching at the onset of the haemorrhage had not clotted. The patient later developed anuria, from which she subsequently recovered.

In the second case the afibrinogenaemia was associated with a ruptured uterus after external version under anaesthesia (Riedel, 1958). This patient died, and the diagnosis of both ruptured uterus and afibrinogenaemia was made in retrospect.

The third case was one of intrauterine death where the admitting house-surgeon noted poor clot formation, and a low fibrinogen level was subsequently confirmed biochemically. The level rectified itself spontaneously, in keeping with the findings of Hodgkinson *et al.* (1955) of fluctuating fibrinogen levels in those cases.

The fourth case is described in some detail, as it illustrates the efficacy of this method.

### ILLUSTRATIVE CASE

An emergency admission was arranged for the patient by her own doctor. He stated that she was a para-1 aged 25, booked for home confinement, who had had a severe ante-partum haemorrhage at 38 weeks' maturity and who was in poor condition. She arrived at 7.30 a.m. in the maternity receiving-room. She was pale and shocked, with a tense, tender uterus, and was losing moderately heavily per vaginam. Her blood pressure was 90/70 mm. Hg and the pulse was feeble and rapid. No foetal heart could be heard. A catheter specimen showed the urine to be solid with albumin. Blood was taken immediately, an intravenous drip of "dextraven" begun, and morphine sulphate, ¼ gr. (16 mg.), given subcutaneously. At 7.45 a.m. one of us (J. A. R.) noted that the sample of blood had not clotted. (Subsequently absence of fibrinogen was confirmed.) The following measures were taken: (1) the dextraven was changed to group O, Rh negative blood; (2) 6 pints (3.4 litres) of blood was ordered from the pathological laboratory; (3) a solution of fibrinogen was prepared; and (4) two bottles of triple-strength plasma were prepared.

At 8 a.m. infusion of triple-strength plasma was begun after the patient had had 1 pint (570 ml.) of blood. Her pulse was still feeble and rapid. Vaginal bleeding continued, and it was noted that this blood showed no signs of clotting. As she reacted with a rigor to the plasma, given at speed, blood was given immediately afterwards.

At 9 a.m. the second bottle of triple-strength plasma was started. Her blood pressure remained low (105/75 mm. Hg), but the pulse had improved in volume and was 90. The blood then showed signs of clotting. A vaginal examination was carried out; the cervix was four fingerbreadths dilated, and the membranes, which were intact, were artificially ruptured. A second 400 ml. of plasma had been given by 9.15 a.m., and spontaneous delivery of a stillborn infant occurred at this time. Ergometrine maleate, 0.5 mg., was given intravenously with the birth of the anterior shoulder; the placenta, which followed immediately, was covered by a large, dark clot of 30 oz. (850 ml.) (supporting the theory that afibrinogenaemia occurs *after* placental separation). Five units of "pitocin" were added to the next pint (570 ml.) of blood, as there was a steady loss and the uterus tended to relax.

At 10 a.m. the fibrinogen was dissolved and ready for administration. By this time the patient had received 4 pints (2.2 litres) of blood and two bottles of triple-strength plasma, and 2.3 g. of fibrinogen in 200 ml. of water was given slowly.

At 11 a.m. the blood clotted normally. The patient's condition was fair, her blood pressure being 100/60 mm. Hg, and there was a slight trickle of blood per vaginam. The pulse was 90 and of good volume. Two more pints (1,140 ml.) of blood were given.

At 5 p.m. her condition was satisfactory; blood pressure 120/80 mm. Hg, pulse 86. The total loss was estimated at 120 oz. (3.4 litres), which had been replaced by 120 oz. (3.4 litres) of blood, and two bottles of triple-strength plasma. That the loss was underestimated was proved two days later, when the haemoglobin (which had been 73% on admission) had fallen to 57%.

The fibrinogen content of the blood was normal 26 hours after delivery, when the clotting-time was 4½ minutes.

### COMMENT

In this case the diagnosis of hypofibrinogenaemia was made within 15 minutes of admission. Fibrinogen replacement had begun 15 minutes later. Within 90 minutes the patient had received 6 g. of fibrinogen (in the form of concentrated plasma) and the blood showed signs of clotting. That, and the measures taken to prevent post-partum haemorrhage, made it possible for the patient to be discharged on the eleventh day, with a normal blood pressure, a trace of albumin in the urine, and a haemoglobin of 67%.

The reasons why we think this method, which is only a slight improvement on the clot-observation test, is worth reporting are: because it is simple and does not need help from a laboratory, because it is applied routinely, and because the diagnosis can be made by an inexperienced house-surgeon soon after admission. Early diagnosis is of prime importance in the treatment of hypofibrinogenaemia.

We thank Mr. K. A. K. Hudson and Mr. A. W. Purdie for permission to report cases under their care.

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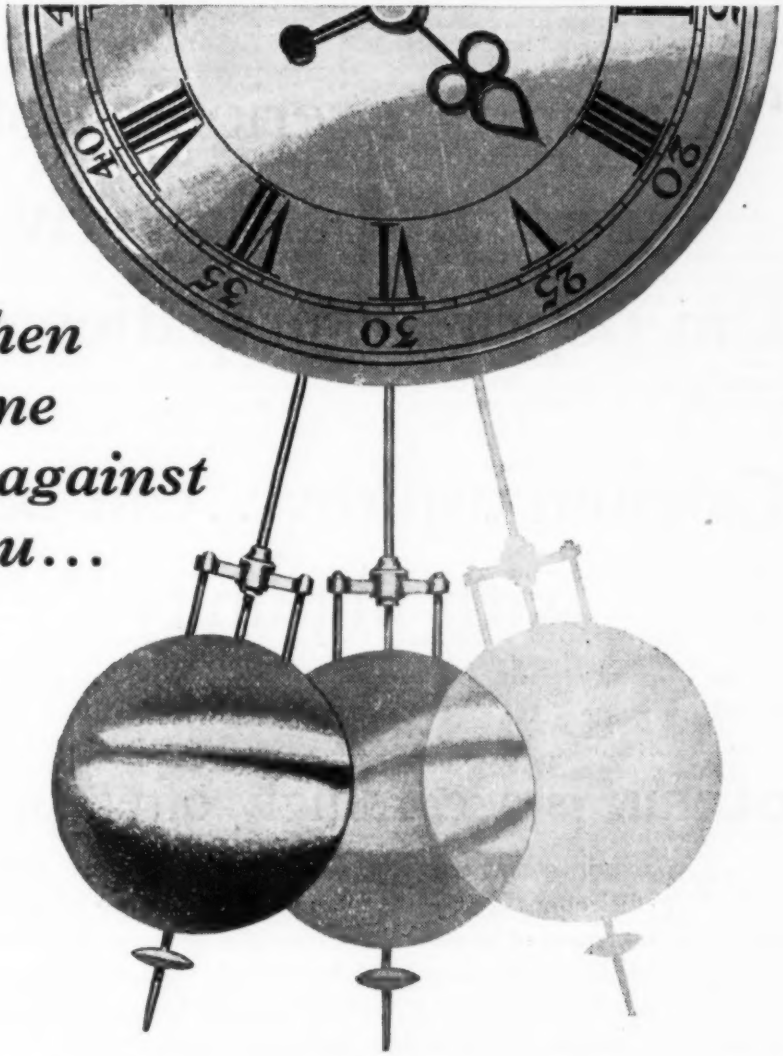

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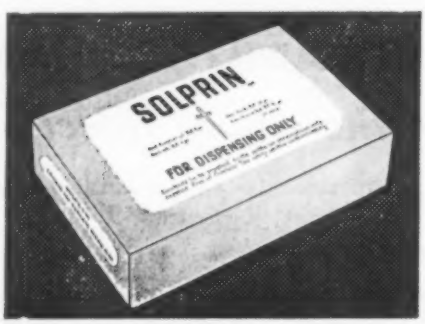


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# Reviews

## MEDICINE AND THE NAVY

*Medicine and the Navy, 1200–1900.* By J. J. Keevil. Volume II—1649–1714. (Pp. 331+ix; illustrated. 40s.) Edinburgh and London: E. and S. Livingstone, Ltd. 1958.

It is indeed fortunate that Surgeon Commander Keevil lived long enough to complete the essentials of his second volume of *Medicine and the Navy*. This volume follows the pattern of the first, presenting a most entertaining and readable account of the development of medicine in England with a naturally naval bias. The theme running through this collection of historical facts might well be founded on the dictum of Lowell that "'Tis man's worst deed to let things that have been run to waste and in the unmeaning present sink the past," for it is a somewhat pathetic story of the obscurantism of the age which could not or would not profit by lessons learnt. The prevention of scurvy among sailors, admittedly empirical, had been found, but 200 years later the medical profession was still unable to connect cause and effect. It may also be salutary for those who decry the National Health Service to realize that it took nigh on 200 years to produce the money to build a naval hospital. History as recounted in this volume undoubtedly repeats itself, for there is a strange, if somewhat ominous, similarity between the frequent "Commissions for Sick and Wounded" of the seventeenth and eighteenth centuries and our modern Commission on the Medical Services of the Crown. The basic reason for these commissions—an attempt to produce the effect of a financial quart out of the Treasury pint pot—is always the same, and it would appear that the results are equally alike.

This volume brings the story up to 1714. It is tragic to realize that Surgeon Commander Keevil, a historian of such outstanding capacity, cannot himself bring the history up to date. We can only trust that the Naval Medical Service will find another "Keevil" to carry on the work of this very gifted and painstaking biographer of the naval surgeons of the past, so that their persistence and perseverance in moulding the evolution of the Naval Medical Service into the highly efficient service of the present day may receive the credit they so richly deserve.

J. C. DOWSE.

## ADVANCED PAEDIATRIC SURGERY

*Pediatric Surgery.* By Orvar Swenson. (Pp. 740; illustrated. $20.) New York: Appleton-Century-Crofts, Inc. 1958.

This book is the work of one who worthily carries on the great traditions of the Boston school of paediatric surgery. His solving of the problem of Hirschsprung's disease is the most important work to come from it since Ladd's classical study of the congenital malrotations of the intestine.

It is significant that in the last few years three detailed, highly instructive, beautifully produced, and very expensive textbooks have appeared on the subject of the advanced surgery of the infant and young child—those of Gross, of Boston; Grob, of Zurich; and now this one of Swenson's. The demand responsible for the appearance of these books springs from a growing realization that many babies and young children are being allowed to die unnecessarily because of the remarkable lack of teaching on this subject in medical education. (Though the Scottish schools, in particular Glasgow, treat it far better than the English.) The whole subject has changed vastly in quite recent times: it is not so long ago that a work on paediatric surgery (Brenner, 1938) began with the words, "The immature organism is predominantly unstable, and this incompetence forbids heroic surgery."

Taking the adjective heroic to mean extensive, we see in all these books that this timidity is entirely unjustified: given the necessary technique, the most drastic and extensive operations can be successfully performed on the youngest and frailest of infants. And it is with technique that Dr. Swenson is particularly concerned; in this respect his book is the most instructive of the three. Because of his own efficiency in this regard he favours immediate end-to-end anastomosis when bowel has to be resected for atresia, or for necrosis in such conditions as intussusception; and it is probably for the same reason that, like other great American surgeons, he dislikes paying the price of added risk for the ease of operating given by muscle relaxants.

He makes the stimulating suggestion that congenital dilatations of the ureters and bladder are caused by defects of the parasympathetic system. Whether or not this is accepted, his method of replacing an inefficient ureter by a segment of surgically narrowed bowel illustrates his technical ingenuity and powers. I am personally flattered by his recommendation of my technique for hypospadias; not surprised by his flat statement that hormone therapy has no place in the treatment of the undescended testicle; and hope that on experiment and reflection he will give up the belief that the cremaster can pull this organ into the inguinal canal.

Like all human works the book has gaps and inequalities of treatment. There is no mention of tonsils and adenoids, nor of spina bifida; the section on hare-lip and cleft palate is poor; and paediatric surgeons in the States have so far been unable to break into the tightly closed shop of the orthopaedists, where it is possible that new advances might result from the approach that has been so successful elsewhere. But the book is a most valuable one for the magnificent treatment of the infant's abdomen and chest, in particular for the section in which the author describes his unequalled experience of Hirschsprung's disease.

DENIS BROWNE.

## METABOLISM OF BONE

*The Chemical Dynamics of Bone Mineral.* By William F. Neuman and Margaret W. Neuman. (Pp. 209+xi; illustrated. 37s. 6d.) Chicago: University of Chicago Press. London: Cambridge University Press. 1958.

There can be fewer subjects in medicine which leave teachers and taught in such an uneasy frame of mind as that of bone metabolism. The original fertile ideas as to calcification processes—such as the calcium and phosphorus product of the plasma, phosphatase and the local factor—have been barely extended since they were originated, and they have subsequently been accepted and developed so glibly by clinicians as to reach the realm of fantasy. This book aims to correct this situation. Its first chapters deal in physico-chemical terms with the modern views of solution chemistry, solubility of bone mineral, crystal structures, and surface chemistry. Heavy going, but an essential corrective in the circumstances. From here on things become more easily digestible by doctors, and the chapters on skeletal dynamics and on physiological regulatory mechanisms are thrilling from the way the authors have developed the basic arguments along more clinical directions. The key factor here is the local citrate concentration and its influence on the product of the ionic activities of $Ca^{++}$ and $HPO_4^{--}$. Both parathyroid hormone and vitamin D can now be plausibly linked with different stages in citrate metabolism, and thus act independently but in the long run synergistically. The final chapter deals critically with the authors' current concept of the calcification mechanism. They firmly reject the generally held view that the local stimulus is due to an increase in calcium and phosphorus product mediated by phosphatase, and prefer to suggest the existence of a local crystal seeding mechanism (epitaxy) probably induced by the organic constituents.

It may appear unfortunate that I cannot withhold a protest against the frequent misspelling in the figures of the standard abbreviations for common terms such as gram and milligram. This slovenliness appears to be increasing in the medical literature of the English-speaking countries, which seems a pity when our spelling conventions have

been internationally agreed to by the entire scientific world, Russia and China included.

The book fills a long-felt gap in the medical literature. Its clear and forthright style makes it easy to read and remarkably stimulating to one's thought processes.

C. E. DENT.

## ADVANCES IN VIRUS RESEARCH

*Advances in Virus Research.* Volume V. Edited by Kenneth M. Smith and Max A. Lauffer. (Pp. 376+x; illustrated. $9.50.) London: Academic Books, Ltd. New York: Academic Press, Inc. 1958.

This is the fifth in a series of annual reviews of advances in virus research. The striking feature of this book is the apt choice of a fundamental subject from each field of virology and the completeness with which each subject is discussed. The first essay, by J. B. Brooksby, on "The Virus of Foot and Mouth Disease," is an up-to-date and full account of the virology of this infection. Mention is made of the geographical distribution of the virus types, but little is said about its epidemiology. Herbert Werner's contribution, "Psittacosis–Lymphogranuloma Group of Viruses," gives a comprehensive account from both the epidemiological and laboratory aspects. Most usefully he emphasizes the large numbers of animal diseases caused by this group and the relation of these animal viruses to human disease. There are two contributions on bacterial viruses. The first, by G. S. Stent, entitled "Mating in the Reproduction of Bacterial Viruses," is a well-studied and extremely interesting theoretical essay based on work on the action of ultra-violet light, radioactive phosphorus, and *x* rays on phages and their host bacteria. The interpretation of Watson and Crick's classical work on the molecular structure of deoxyribose nucleic acid is modified to explain his observations. Using four phages as models, G. Bertani gives a lucid and factual account of lysogeny. A lengthy discourse is given by Ph. L'Heritier on the "Hereditary Virus of *Drosophila*," with special emphasis on the action of $CO_2$ on the infected insects and the transmission of this virus. There has been an outstanding requirement for a review on the measurement of complement-fixation by viruses. This has been amply fulfilled by Forrest Fulton's article. Each component of the test has been fully dealt with, and their application in three dimensions as antigen, antiserum, and complement contours described. The author has tackled a difficult subject and has attempted to clarify it by a mathematical approach. The last contribution, "The Mechanism of Hemagglutination by Influenza Virus," is by A. Buzzell and M. Hanig. This is a detailed review of the subject; nothing important has been omitted, and it is written so concisely and clearly that all who work with influenza will find it invaluable.

P. S. GARDNER.

## THE DISCOVERER OF STREPTOMYCIN

*My Life with the Microbes.* By Selman A. Waksman. (Pp. 320. 21s.) London: Robert Hale Ltd. 1958.

Although it is true that the great discovery comes to the mind prepared, it is also true that there are many different ways of preparing the mind. Fleming's mind was trained to appreciate the value of the chance observation, but Dr. Waksman had prepared himself for the discovery of streptomycin by knowing more about soil bacteriology, and particularly the influence of the members of this teeming microbiological population upon each other, than anyone else in the world. His researches conducted for 20 years had shown, as early as 1936, that actinomycetes were able to exert a considerable influence on the growth and activities of fungi and bacteria in the soil. The discovery of streptomycin in 1943, therefore, following the discovery of penicillin by Fleming, was no more than the climax of these researches, for it was prepared from an organism, *Actinomyces griseus*, first isolated by himself and a collaborator in 1915.

Dr. Waksman emigrated from Russia to the United States in 1910, and has been since 1918 on the staff of the College of Agriculture at Rutgers University in New Jersey. The University had made an agreement with Merck and Co. in 1939 that all patentable processes should be assigned to this firm in exchange for a royalty of 2½% and for considerable scientific help provided by Merck's. After the discovery of streptomycin Merck's agreed that other interested organizations should be allowed to manufacture it under arrangement similar to that made with themselves.

Some of the interest of Dr. Waksman's excellent autobiography is to be found in his story of the complicated relationships that crowd upon the discoverer in the modern world—relations not only with his employing university and with manufacturers, but also with the press and the public, with patients both gratified and disappointed, and even with his assistants. A former student instituted a legal suit for a share of the large profits; he was paid 125,000 dollars for the assignment of all foreign patent rights and 3% of the royalties. Whereupon Dr. Waksman, whose judgment and good will were not submerged by these legal complications, decided that half his share in the royalties—namely, the 10% which he had returned to the Rutgers Research and Endowment Foundation—should be distributed among the 26 of his former students and assistants who had helped in the development of the antibiotics programme. The law is now prepared, not only to assess the financial value of an erring wife, but also to judge the contribution made to a great discovery by the laboratory assistant who prepares the culture media. A friend of mine when receiving an award for his researches said, "The prestige I gladly share with my assistants; the money I will keep for myself"—a simple and old-fashioned solution of a problem which has now acquired a new look.

D. V. HUBBLE

## PERIPHERAL CIRCULATORY DISTURBANCES

*Begutachtung Peripherer Durchblutungsstorungen.* By H. W. Passler and H. Berghaus. (Pp. 272+xi; illustrated. DM.45.) Stuttgart: Georg Thieme Verlag. 1958.

This book on the examination of peripheral disturbances of the circulation is based on 100 well-documented cases. Investigation by serial angiography is found to be very important. There are a number of excellent photographs of the vessels of the legs obtained in this way. The author claims that it is absolutely safe. The campaign in Russia provided an enormous amount of material for the study of the effect of cold on the vascular system. The author had special opportunity to investigate these cases. The effect of cold is considered in both healthy and diseased arterial systems. Deficiency states are dealt with, and the effects of trauma. In another section the effects of peripheral disturbance of the venous circulation are considered. The numerous cases are well described and shortly presented. The illustrations are excellent. There is a full list of references. The print and index are clear and adequate. Altogether an up-to-date and efficient presentation of an important subject. The book can be heartily recommended. As the title implies, there is nothing about therapeutics.

TERENCE EAST

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*Centenary of the General Medical Council, 1858–1958* (pp. 31 +2 plates, published by the Council, 3s. 6d.) gives an account of the history and present functions of the G.M.C. compiled by Mr. Walter Pyke-Lees, its present Registrar. After a brief note on the events leading up to the Medical Act of 1858, which brought the Council into being, Mr. Pyke-Lees describes the difficulties encountered in the preparation of the first *Medical Register* and *British Pharmacopoeia*. He also discusses the Council's efforts from time to time to promote legislation for the better discharge of its functions. The Council's duties in the field of medical education—not always appreciated—are shown to be one of its major concerns; it has devoted much time to examination and revision of the curriculum. Its disciplinary powers, it is pointed out, are not intended to be retributive, but are for the protection of the general public. In the words of Sir Donald MacAlister, an outstanding past-president, the Council's two great functions are "to prevent the unfit from gaining access to the Register, and . . . to remove the unworthy from it."

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SATURDAY DECEMBER 13 1958

## B.M.A. CLINICAL MEETING

The candid, and usually caustic, critic of the B.M.A. is never tired of saying that an organization which costs over a quarter of a million pounds a year to run spends too much of its energy on getting more money for doctors. Those who report the A.R.M. in the press sometimes accuse our spokesmen of talking money instead of medicine, of what they can get out of the country instead of what they can give it. Since 1948 the B.M.A., the critic says, has taken on too much of the colouring of a trade union —too much, at least, for the liking of many of its members. The worst consequence of the N.H.S. is that it has made doctors too self-conscious about money. And small wonder ! The gay promise of the Spens Reports has not been fulfilled. What seemed a decent enough charter has been turned by politicians and the quibblings of civil servants into a dirty piece of paper. Not insensitive to all this, those responsible for the conduct of B.M.A. affairs have this year, and last week, instituted the first Annual Clinical Meeting. It was held in Southampton from December 4 to December 7. It was an annual meeting of the B.M.A. in which the words Spens, Danckwerts, capitation fee were neither uttered nor published. It was, refreshingly and hopefully, a meeting at which men and women spoke and thought solely of their work, of clinical medicine and scientific investigation. It was a meeting of doctors.

Panel discussions, general sessions, colour television, medical films, clinical demonstrations in the hospitals of Southampton, filled out the day, with short respites for lunch and tea. There was a big attendance of doctors from the neighbourhood and from further afield, and many distinguished physicians and surgeons came from as far north as Edinburgh to join in this feast of reason and good fellowship. A large audience saw a magnificent demonstration of a " live operation " for atrial septal defect colour-televised from Southampton General Hospital. The other *coup de théâtre* was the Transatlantic Clinical Conference between a British group in the Guildhall of Southampton and a team from the U.S.A., at the American Medical Association's Clinical Meeting in Minneapolis. There were two cases for diagnosis, and only one member of each team knew the answer for his own side. It was, certainly, at least for the British, a dramatic occasion. Two to three hundred British doctors in Southampton Guildhall participated in a clinical conference between four British and three American doctors separated by four thousand miles. Medicine certainly is not dull, and no one who listened in will ever again see a case in which there is an excess of gammaglobulins in the blood without thinking of myxoma of the atrium.

The Southampton meeting was a success, and any fears its sponsors may have had on this score were soon laid to rest. Drs. R. S. Russell-Smith, J. G. McDowell, and R. P. W. Shackleton, who laboured so mightily in their home town to make the meeting what it was, must now feel justifiably content. And so must be the chairman of the Committee of Management, Dr. Ronald Gibson, untiring in his efforts to weld the B.M.A. into a unity of like-minded men and women whose common meeting-ground must always be the art and craft and science of a great and inspiring vocation. As Professor A. P. Thomson, the B.M.A.'s President said last week, the Southampton Clinical Meeting has set a standard and example for the future. The next meeting will be in Norwich a year from now. Maybe less time should be given to the set lecture in the general session and more to panel discussions and clinical demonstrations. What is surely needed is active participation, and it was curious how this was felt at the Transatlantic Clinical Conference. Everyone present was silently taking part and making his own diagnosis. The lecture, however, puts the listener too far back into the passive receptivity of the student furiously scribbling notes on a hard bench. But the pattern set at Southampton, if not perfect, was little short of excellent, so excellent that some hope that a spring and an autumn clinical meeting on the Southampton model might be separated from the Annual Representative Meeting, which itself could be held regularly in the summer in the Parliament of the B.M.A.—B.M.A. House, Tavistock Square.

## PERIPHERAL NEUROPATHY AND THE LUNGS

Over the years a formidable list of causes of peripheral neuropathy has grown up. It includes chemical agents, metabolic disorders, and infective states. In many diseases the neuropathy is a well-established component or complication—for example, poisoning by heavy metals, diabetes mellitus, vitamin-B deficiency, and diphtheria. In others it occurs infrequently and is usually ascribed, for want of a better

explanation, to a "toxic" cause. Occasionally it develops in conjunction with respiratory disorders, and many attempts have been made to discover a specific relationship between the lungs and the peripheral nerves. These have not been entirely unsuccessful. For example, peripheral neuropathy and carcinoma of the bronchus would seem at first sight to make uneasy bedfellows, but their association has been proved to be real beyond doubt.[1] Of the infections, perhaps advanced tuberculosis is the best known, but transient neuropathies may complicate pneumonia and influenza, and two instances of rather severe chronic peripheral neuropathy have recently been recorded in bronchiectatics, the neurological features being relieved in each by effective treatment of pulmonary suppuration.[2]

In trying to relate the pulmonary condition to the neuropathy, the problems posed by carcinoma and the infections are different. The mechanism of the association with carcinoma remains a complete mystery, whereas the main issue with the infections is to decide whether neuropathy occurs more frequently with inflammation of the lungs than it does with inflammation elsewhere in the body. A consideration of the clinical aspects strongly suggests that such mechanisms as may be involved are dissimilar in the two pulmonary conditions.

The first manifestation of carcinoma may precede, coincide with, or follow the neurological signs. The tumour is often situated peripherally and its size bears no relation to the degree of neuropathy. The neuropathy runs a variable course, sometimes becoming arrested or remitting spontaneously and usually being unaffected by surgical removal of the growth. Hence any causative link seems to act in a haphazard way. In seeking an explanation, many suggestions have been made. Intoxication by arsenic springs to mind as an obvious common factor, but no evidence of excessive exposure to arsenic has ever been found in these cases. The possibility of a virus being responsible for both seems improbable, since it would be likely to act upon the nerves within a matter of weeks, whereas a carcinoma would take much longer to develop. Metabolic disorders are very difficult to assess because of their complexity, but vitamin therapy rarely if ever relieves the neuropathy; disturbances of pantothenic-acid metabolism or even the production of an anti-vitamin substance by the carcinoma cells have been mentioned.[3] Nervous reflexes from the lungs might conceivably play a part.[4] In other words, we do not know, even to the extent of which system may provide the link.

Many acute infections are known sometimes to be associated with peripheral neuropathy—for example, septicaemia, puerperal sepsis, mumps, measles, smallpox, scarlet fever, gonorrhoea, syphilis, meningitis, typhoid, paratyphoid, dysentery, typhus, malaria, influenza, and pneumonia. The neurological features ordinarily develop during or shortly after the febrile phase, and no evidence exists suggesting that pulmonary involvement *per se* predisposes to peripheral neuropathy. The question whether chronic infections are more likely to do so if situated in the lungs rather than elsewhere is less certain. Peripheral neuropathy has been observed in advanced phthisis, chronic suppuration of the extremities,[5] osteomyelitis,[6] and bronchiectasis.[2] These are toxic and debilitating diseases which may easily disorganize metabolism to the extent of interfering with the nutrition of the peripheral nerves, possibly with amyloidosis in addition, but again no specific pulmonary mechanism seems to be acting. However, the recent publication of two cases of bronchiectasis with peripheral neuropathy and no evidence of cachexia or metabolic upset[2] is perhaps a straw in the wind; the publication of further similar cases must be awaited before a firm conclusion can be drawn.

[1] Lennox, B., and Prichard, S., *Quart. J. Med.*, 1950, **19**, 97.
[2] Caughey, J. E., Wilson, R. F., and Borrie, J., *Thorax*, 1958, **13**, 59.
[3] Denny-Brown, D., *J. Neurol. Psychiat.*, 1948, **11**, 73.
[4] Wyburn-Mason, R., *Lancet*, 1948, **1**, 203.
[5] Schmidt, C. P., *Nervenarzt.*, 1948, **19**, 81.
[6] Lebedev, A. P., *Vestnik Khir.*, 1953, **73**, 55.

## INSULIN ANTIBODIES

Insulin resistance is a well-known phenomenon in diabetes mellitus. It may occur temporarily during infections or ketosis, and is a common finding in the obese diabetic and in the patient who has diabetes in association with acromegaly or Cushing's syndrome. Occasionally patients need enormous doses of insulin to control the disease. Several mechanisms have been suggested to explain this resistance. Antagonism of insulin by growth hormone, and particularly by adrenal steroids, might well be expected, but except in the endocrinopathies has not been proved. It is known that the liver contains an enzyme insulinase which destroys insulin, and that this enzyme in its turn is acted upon by insulinase inhibitors.[1] It is not yet clear, however, what part this complex plays in the diabetic syndrome. A third possibility is that certain patients develop antibodies to insulin. This has been suspected for some years,[2]

[1] Mirsky, I. A., *Metabolism*, 1956, **5**, 138.
[2] Lowell, F. C., *J. clin. Invest.*, 1944, **23**, 233.
[3] Pressland, J. R., and Todd, C. M., *Quart. J. Med.*, 1956, **25**, 275.
[4] Berson, S. A., Yalow, R. S., Bauman, A., Rothschild, M. A., and Newerly, K., *J. clin. Invest.*, 1956, **35**, 170.
[5] Berson, S. A., and Yalow, R. S., *Diabetes* 1957, **6**, 402.
[6] Burrows, B. A., Peters, T., and Lowell F. C., *J. clin. Invest.*, 1957, **36**, 393.
[7] Skom, J. H., and Talmage, D. W., ibid., 1958, **37**, 787.
[8] Kalant, N., Gomberg, C., and Schucher, R., *Lancet*, 1958, **2**, 614.
[9] Yalow, R. S., and Berson, S. A., *J. clin. Invest.*, 1957, **36**, 648.
[10] Randle, P. J., and Taylor, K. W., *Lancet*, 1958, **2**, 996.

though their presence cannot always be detected by the usual immunological techniques. Nevertheless the presence of insulin antagonists in the serum of resistant patients can be shown by various indirect means, such as the protection afforded to animals receiving lethal doses of insulin and the effect on the uptake of glucose by the rat diaphragm[3]

Renewed interest in the role of antibodies has been stimulated by recent studies of the fate of insulin labelled with radioactive iodine.[4] It has been found that treated diabetics retain insulin-$^{131}$I in the circulation longer than those who have never received insulin, and that the radioactivity is concentrated in the globulin fraction of the plasma proteins. Such insulin binding, presumably in the form of an antigen–antibody complex, is an invariable response to repeated insulin injection, but its relation to the development of resistance is not at all clear. Thus, while some workers[5,6] have found much greater binding in insulin-resistant patients, others[7] have been unable to show any connexion between the degree of insulin binding and the dosage and duration of treatment. N. Kalant and colleagues[8] have concluded that neither retention of radioactive insulin in the serum nor the degree of binding affect the response to a given dose of insulin. Moreover, the serum of animals actively immunized to the hormone does not exhibit insulin-neutralizing activity, nor do such animals show any great diminution in responsiveness to insulin. They suggest that repeated injection of insulin leads first to a decrease in its rate of degradation, followed later by the appearance of circulating antibodies in the form of a loose complex which does not necessarily interfere with the action of insulin. A further factor which may partially explain why the presence of antibodies is not clearly linked to insulin resistance is the ability of serum from treated diabetics to inhibit insulinase.[9]

A full interpretation of the phenomenon of insulin binding must await further work on the metabolism of insulin, both in normal subjects and in diabetics. It is possible, for example, that a similar mechanism occurs in the serum of healthy people,[10] and that the insulin-globulin complex is not an immunological response in the strict sense. The fact that it always appears in the treated diabetic suggests that it has little to do with insulin resistance. Similarly it seems unlikely that such a mechanism would influence the long-term insulin requirements of the average patient. Yet it is possible that the development of antibody would tend to increase the dose required for a given effect,[7] and this would explain the resistance that occurs in patients receiving insulin-shock treatment.

## MORBIDITY IN GENERAL PRACTICE

During the twelve months from May, 1955, to April, 1956, 171 general practitioners in more than 100 practices in England and Wales kept clinical records of all their Health Service consultations. This survey of the morbidity encountered in general practice was conducted jointly by the General Register Office and the College of General Practitioners, and the first volume of results has now been published.[1] Two more are promised. There are few comparable studies, though the rich rewards that can be won from careful observation in general practice have been brilliantly shown by Budd, Mackenzie, Pickles, and others. There was an obvious need for more information of this sort; an earlier pilot study from the General Register Office showed that it was well worth collecting[2,3]; and epidemiologists, public health officers, and general practitioners have been awaiting the results of this large study with the keenest expectation.

The survey is based on two items of information—the consultation between doctor and patient, and the diagnosis of the patient's complaint. More than half the book consists of tables presenting this basic information differentially by sex, age group, and geographical area. Two different types of rate have to be distinguished: the "consultation rate" measures the numbers of times a patient was seen by his doctor for a particular disease; the "patient-consulting rate" is the number of patients suffering from a disease, regardless of the number of consultations. It is unfortunate that the two names are so similar and are not self-explanatory so that it requires a little mental effort to hold them in mind while studying the tables. The patient-consulting rate is held to give a truer picture of the amount of sickness in the community because doctors will differ widely in the number of consultations which they give to a patient for a particular illness. Nearly 400,000 patients were seen by the doctors and the number of consultations reached nearly 1¼ million.

The early chapters give details of the methods adopted to ensure completeness and uniformity in the data. Sometimes arbitrary decisions had to be made on how to deal with recurrent diseases; for example, whether each attack of asthma should be considered separately or as a continuation of a single disease. The devices for recording several diseases at a single consultation and for linking subsequent consultations with previous ones for the same disease are ingenious.

The book is so arranged that it will be invaluable to anyone planning similar investigations, and it is so complete that it would not be difficult to repeat the survey in every respect. The later volumes will show in more detail what inferences can be drawn from these tables, but the present volume gives certain interesting statistics. For example, only 30% of female patients did not consult their doctor during the year, whereas 37% of males kept away. One would have expected a larger discrepancy. The proportion of patients seen was

[1] *Morbidity Statistics from General Practice*, Vol. 1 (General), 1958, H.M.S.O., 15s 6d.
[2] *General Practitioners' Records*, 1953, H.M.S.O.
[3] *Brit. med. J.*, 1953, **2**, 1038.

higher in the age group under 15 years, but the elderly patient tended to be seen twice as often as the average child or young adult. The number of patients consulting for malignant disease was 5.2 per thousand, suggesting a total of approximately 230,000 cases of cancer under treatment in the whole country. Those interested in psychoneurotic disorders will find that the patient-consulting rate for these was 45.7 per thousand, indicating a national total of 2,000,000 patients under the care of their doctor during that year, or one in twenty of the population. The common cold gave the highest patient-consulting rate for individual diseases, 81.1 per thousand, though it entailed fewer consultations than this rate would suggest, and it was bronchitis that most often required medical attention. With a consultation rate of 261.1 per thousand and a patient-consulting rate of 62.3 per thousand, bronchitis had the third highest patient-consulting rate, coming after arthritis-and-rheumatism with 64.9 per thousand. Surprisingly, influenza came fifth on this list, both for patient-consulting rate and for consultation rate, though there was no great influenza epidemic in that year.

High praise must go to Dr. W. P. D. Logan and his team at the General Register Office, to the general practitioners, their secretarial staffs and probably their wives, for the fine work which has produced this volume, and the care and skill with which it has been written. Still higher praise must go to those general practitioners who were able to offer an account of the occupation of all their patients. It requires much work to obtain the full statistics of sex and age for a general practice, and to add to this the occupation of the patient is a formidable undertaking. A sufficient number of general practitioners, nevertheless, did so to make possible an analysis of sickness in relation to occupation which is promised for a subsequent volume. The present work whets the appetite for what is to follow, and everybody interested in epidemiology and morbidity figures will want to collect the series.

## IMAGE INTENSIFICATION AIDED BY TELEVISION

In diagnostic radiology an *x*-ray image is usually rendered visible by allowing it to fall on some material which converts *x* rays into light (a fluorescent screen) or on to a photographic film which, on processing, reveals the latent image; or a combination of these two methods may be used. Image intensification refers to any electronic method which enables the film or fluorescent image to be obtained with a reduced quantity of *x* rays. There are many reasons for wishing to reduce the dose of radiation, the potential hazards being in themselves a cogent one. The present methods of image intensification are first to convert the *x*-ray image into a light image with the use of a fluorescent screen and then to convert the light image into an electron image. The energy of the electrons is then increased and the image may be focused with electron lenses and allowed to fall on another fluorescent screen yielding a considerably brighter image than the first one. Alternatively, the initial image may be scanned as in television, the resultant electric current being then amplified and viewed on a conventional television screen as an image with increased brightness. In either case the image may be photographed, but the television system has the advantage that contrast can be varied at will. The use of equipment of this type, which is available commercially in the U.S.A., has been described by R. H. Morgan and R. E. Sturm[1] and by R. Janker.[2] For medical purposes, however, the radiologist is primarily concerned with obtaining a brighter image with less radiation and without significant reduction of definition rather than with achieving merely increased brightness with the same doses of radiation as are used with conventional methods. Unfortunately, when the quantity of *x* rays required to give a fluoroscopic image is significantly reduced, the definition of the image falls because of statistical fluctuation of the *x*-ray quanta on these low levels.[3] This means that, though it may be possible to intensify the image without increasing the dose of radiation, so far it has not been possible to maintain definition in the intensified image with doses of radiation much less than those used at present. It seems unlikely that further advances of major importance can be made in this field unless a more efficient means than the fluorescent screen is found for converting the primary *x*-ray image, for, though image intensifiers may have an intensification factor of hundreds, the radiologist can reduce the dose of radiation only by units. However, improvements sufficient to make the method useful in practice may result from comparatively small refinements in any of the components of the system. These problems are being investigated in several centres, including the department of instrument technology of the Imperial College of Science and Technology, London, and their solution will be eagerly awaited by radiologists.

[1] Morgan, R. H., and Sturm, R. E., *Radiology*, 1951, **57**, 556.
[2] Janker, R., *Fortschr. Röntgenstr.*, 1958, **88**, 377.
[3] Sturm, R. E., and Morgan, R. H., *Amer. J. Roentgenol.*, 1949, **62**, 617.

## QUALITY OF DRINKING-WATER

In this age of standardization it is not surprising that the quality of water for domestic consumption has been under consideration. Both in Great Britain[1] and in the U.S.A.[2] there have been standards for many years, but the first attempts to obtain international agreement were at the Congresses of the International Water Supply Association in Amsterdam in 1949 and in Paris in 1952. Little progress was made, and so the matter was taken up by the World Health Organization, which had long appreciated the need for some form of international agreement on the requirements for safe and potable water supplies. This problem has become more acute with the great increase in travel, especially air travel, "where common carriers must be watered at many points in the world, and the traveller must be furnished with acceptable drinking-water that will not produce unfavourable effects on his health."[3] Groups of experts,

each one representing a member state of the World Health Organization, studied these questions at a regional level between 1953 and 1956. The unanimity attained exceeded expectations, and a final study group therefore met in Geneva in the summer of 1956. It has put forward detailed recommendations applicable the world over.[3] This report is intended primarily to refer to water as it is supplied to the public.

The introduction to this important publication states that "supplies of drinking-water should not only be safe and free from dangers to health, but should also be as aesthetically attractive as possible. Absence of turbidity, colour, and disagreeable or detectable tastes and odours is important in water supplies intended for domestic use." The requirements for providing water of this quality are set out in successive chapters discussing bacteriological, chemical, physical, biological, and radiological requirements. The standards of bacteriological quality recommended are not as strict as might be, but there are many areas in the world where the regular attainment of a standard of coliform organisms absent in 100-ml. volumes is not economically or technically practicable. Different standards are set down for treated and untreated supplies for present use throughout the world, with the hope that improvement in economic and technical resources will permit of stricter standards being adopted at a later date. Limits for toxic substances such as lead, arsenic, and cyanide in the water are given, and also for specific substances, such as fluoride and nitrate, which may affect health. Many other chemical substances affect the potability of water, but, owing to the wide variation in chemical composition of water in different parts of the world, rigid standards cannot be laid down. What has been done is to designate limits for such substances as iron, copper, zinc, sulphate, chloride, and so on which are "permissible"—that is, would be generally acceptable by consumer—and "excessive," values greater than which would eventually impair the potability of the water.

But this publication is not a mere list of standards. Many aspects of water quality are fully discussed and details of sampling procedure are set out in the appendices, together with approved methods of analysis. Moreover, since standards and analytical methods are not static, but must change with advances in knowledge, a list of subjects for future research is included. Finally, the frequency of sampling, particularly bacteriological, is worth mentioning. The report rightly attaches importance to this procedure and gives a sound guide for sampling before and after the water has entered the distribution system. To get water to the consumer without any deterioration in quality, a close watch has to be kept on the network of mains, pipes, and reservoirs —the "Achilles heel" of a water undertaking. Regular sampling and analysis is one way of checking the distribution system, and the W.H.O. experts have proposed a practical programme of routine control to this end.

[1] Ministry of Health and Ministry of Housing and Local Government, England and Wales, *The Bacteriological Examination of Water Supplies*, 1956, 3rd ed. London. H.M.S.O. (Reports on Public Health and Medical Subjects No. 71.)

[2] American Public Health Association, *Standard Methods for the Examination of Water, Sewage and Industrial Wastes*, 1955, 10th ed. New York.

[3] World Health Organization, *International Standards for Drinking Water*, 1958, Geneva.

## TREATMENT OF ASTHMA WITH HYDROCORTISONE POWDER

The success of steroid therapy in carefully chosen cases of chronic asthma, coupled with its undoubted and serious risks, has led investigators to try the effect of these drugs in smaller dosage when applied locally to the bronchial mucosa by means of some form of oral inhalation. W. S. Foulds[1] and his colleagues reported an uncontrolled trial of hydrocortisone snuff on 15 patients, of whom 12 improved. H. Herxheimer and M. McAllen[2] found that in 4 out of 10 patients with pollen asthma the symptoms disappeared after nasal insufflation of hydrocortisone snuff. R. M. Morris-Owen and S. C. Truelove[3] made a similar observation. W. Brockbank and C. D. R. Pengelly,[4] using a very small dosage, reported improvement in 17 out of 24 asthmatics with inhalations of hydrocortisone acetate powder, but when prednisolone was used there was no effect in 6 out of 7. W. H. Helm and F. Heyworth[5] have recently conducted a short-term blind-controlled trial of inhalations of hydrocortisone acetate in 26 patients, prescribing up to 45 mg. a day. 14 out of 17 improved, but only 3 out of 9 showed benefit when an inert powder was given. They concluded that these inhalations were an effective form of short-term treatment in some cases of bronchial asthma. In a second paper[6] they described the effect of treating 53 patients in a similar way, 81% showing improvement. But there was a strong tendency to relapse if treatment had to be maintained. Prolonged benefit was more likely to occur if the inhalations were given intermittently for recurring asthmatic attacks. They also determined that there was a wastage into the stomach of about 20% of the powder.

Herxheimer[7] and his colleagues have described three trials of similar treatment in London, Cardiff, and Berlin, but do not state what salt of hydrocortisone was used. The dosage was one 15-mg. capsule administered daily, half in the morning and half in the evening. Although more than two-thirds of the patients benefited, the results need interpreting with caution. Some of them were a selected group and seemed likely to respond before treatment began, and did so. In contrast, the Cardiff study was of unselected cases, and there the number of failures (19) exceeded the number of successes (15). This treatment cannot therefore be expected to relieve the average chronic asthmatic, but only certain types. Herxheimer and his colleagues endeavoured to analyse the types that seemed to derive most benefit from the treatment. It is not surprising to find that those with excessive secretion failed to respond. The improvement occurred in patients with evidence of

[1] Foulds, W. S., Greaves, D. P., Herxheimer, H., and Kingdom, L. G., *Lancet*, 1955, 1, 234.

[2] Herxheimer, H., and McAllen, M., ibid., 1956, 1, 537.

[3] Morris-Owen, R. M., and Truelove, S. C., *Brit. med. J.*, 1958, 1, 969.

[4] Brockbank, W., and Pengelly, C. D. R., *Lancet*, 1958, 1, 187.

[5] Helm, W. H., and Heyworth, F., *Brit. med. J.*, 1958, 2, 768.

[6] —— —— ibid., 1958, 2, 765.

[7] Herxheimer, H., McAllen, M., and Williams, D. A., ibid., 1958, 2, 762.

allergic aetiology and those without hypersecretion. Cases of dry asthma responded dramatically. In Helm and Heyworth's[6] study cases of recurrent acute asthma without significant bronchial infection responded best, while cases of wheezy bronchitis with significant infection and more than ½ oz. (7 ml.) of sputum daily responded least. This important work is worth following up. It is an ideal piece of research for the busy general practitioner.

## SEBORRHOEA

In the last two decades there has been much study of the structure and function of the skin, particularly of the epidermis and its appendages and the surface film, or "mantle of the skin." Much of this work has been done in the United States and has been summarized in the two important textbooks of S. Rothman[1] and W. Montagna.[2] The great importance of the skin in relation to general metabolism and the reflection of systemic disease in the skin steadily assume greater importance in medicine; it is, moreover, an organ that should be susceptible of more exact study than those hidden beneath the surface. The integrity of the skin is important as a barrier against injury from without, mechanical, chemical, climatic, or infective, and this integrity is in part dependent on humoral and endocrine influences. Emphasis is now placed on the equipotentiality of epidermal cells—the ability of any epidermal cell to produce any element of the surface epithelium or of its appendages.

Much has yet to be discovered about the process of cornification or keratinization, but much is known about the surface film. Marchionini long since stressed the variation in hydrogen-ion concentration of the surface film at different sites on the skin surface and under different conditions, and Rothman has shown that the character of skin fats in the film may vary with different diseases and may bear upon the causation of those diseases.

The surface film is dependent for its effectiveness not only on sebaceous and apocrine secretion but on the fats and waxes provided by the desquamating horn cells, and the whole is emulsified by the contribution of the sweat glands, which, for instance, carry sebum readily over the palms and soles where no sebaceous glands exist. The contribution of the sebaceous glands is enhanced by the advent of puberty when apocrine glands also begin to function, and throughout adult life endocrine influence is paramount. It is at puberty that the surface film spontaneously destroys the *Microsporum audouini* fungus on the scalp as a consequence of the increased secretion of the long-chain saturated fatty acids. But this is only one aspect of the seborrhoeic diathesis, itself a reflection of a physiological state dependent on genetic, emotional, and other factors besides the endocrine.

J. M. Beare and colleagues[3] have recently studied the *p*H of the skin surface in infants suffering from seborrhoeic dermatitis, and believe that the difference from that of normal control subjects is sufficient to be of value in differential diagnosis in difficult cases. Their investigations have been carefully controlled statistically and show that in seborrhoeic dermatitis in infants the surface film is more alkaline than in the normal. The incidence of seborrhoeic dermatitis in infants varies considerably with geographical location and nutritional state, but it is a mild affection that clears readily with treatment, or spontaneously, unless it triggers off a constitutional eczema. The seborrhoeic state is not, in fact, natural to the human until puberty, and its occurrence in infancy—sometimes with a phase of acne vulgaris—is probably dependent on hormonal influences carried over from the mother which disappear in the course of the first few months of life.[4] The findings are of interest because the active state of seborrhoea at puberty and the seborrhoeic diathesis in the adult are generally regarded as being associated with an abnormally acid secretion. These features are related to the bacterial and fungal activity on the skin surface, and further investigations on these lines would be welcome.

## THE EDINBURGH MEETING

Next year's Annual Meeting of the British Medical Association looks like being an invigorating affair. For one thing it is to be a Joint Meeting with the Canadian Medical Association, and those who went to Toronto in 1955 know what a stimulating experience it is to forgather with our Canadian colleagues. For another thing the meeting is to be in Edinburgh, one of the few big cities in the world where history, culture, and learning still hold out against industry and commerce. The arrangements for the meeting are well in hand, and this week's *Supplement* contains the provisional programme. As can be seen, the scientific meetings cover a very extensive field, and the opportunity to hear the views of so many experts from both sides of the Atlantic is one that will seldom recur. Edinburgh being what it is, the social occasions are also likely to be memorable, and the wives and families of members will all be made welcome—in fact, special arrangements are being made for the entertainment of young people.

Both the British and Canadian Medical Associations will have Prince Philip, Duke of Edinburgh, as their President next year, and, though he will be in Canada with the Queen at the time when the Annual Meeting is taking place in Edinburgh, his acceptance of both Presidencies brings the two Associations into even closer harmony than before. The Joint Meeting will certainly attract great numbers of doctors and their families to Edinburgh next July. Therefore, since the holiday season will be well under way, members who are in a position to do so would be well advised to book their accommodation in Edinburgh now, and also to make their train reservations.

[1] Rothman, S., *Physiology and Biochemistry of the Skin*, Chicago, 1954.
[2] Montagna, W., *The Structure and Function of the Skin*, New York, 1956.
[3] Beare, J. M., Cheeseman, E. A., Galley, A. A. H., and Neill, D. W., *Brit. J. Derm.*, 1958, **70**, 233.
[4] Ingram, J. T., *A.M.A. Arch. Derm. Syph.*, 1957, **76**, 157.

*Drug Treatment of Disease*

# DISSEMINATED SCLEROSIS

BY

**MICHAEL KREMER, M.D., B.Sc., F.R.C.P.**

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It is still unfortunately true that there is no specific remedy in disseminated sclerosis, but it would be very wrong indeed for this reason to abandon these patients without treatment of any kind, for much can be done to give symptomatic relief. As important as anything else in the treatment of this condition is the attitude of the doctor. There is still some ignorance in the profession of the natural history of the disorder, and once the diagnosis is made a feeling of pessimism may overwhelm the practitioner, who feels he is faced with a hopeless patient soon to be reduced to a life of chronic incapacity and needing almost full-time care. That this is not the case is by no means sufficiently widely known.

The frequency of the disease in Great Britain is about one in 2,000 of the population; it varies in different counties. There are therefore a large number of sufferers, and it is clear at once that there are not that number of severely incapacitated patients in this country suffering from disseminated sclerosis. Many of these patients have long periods of remission often lasting many years. There are others whose disorder is mild, and, while they may have many abnormal signs in the nervous system, yet disorder of function and impairment of useful life are slight.

An explanation to the intelligent patient along these lines may be very helpful; it may prevent him from feeling that the doctors are abandoning him and stop him and his relations from wandering round seeking help which is not available.

## Lines of Attack

Many treatments of the disease have been tried, but assessment of results is impossible except on a very long-term basis, as any therapy may coincide with a natural remission. The major lines of attack are as follows.

*Vaccines.*—The latest of these is the Shubladze-Margulis vaccine from the U.S.S.R. There is no evidence yet available that this has any effect on the disease and it is possible that the substance is dangerous. Bacterial vaccines, usually autogenous, have been tried, and these too have not been accepted as producing any relief.

*Pyrexia.*—Before the second world war there was a great vogue for pyrexial treatment. The pyrexia was induced by the use of killed organisms, such as T.A.B. vaccine, intravenously, and the patient was allowed to have up to six or even more bouts of fever. But in recent years this method of treatment has been used less and less. There is no doubt that it could initiate a remission for a time.

*Vasodilators.*—This is a useful method of treatment and may be of considerable help in bringing a relapse to an end rather sooner than would otherwise happen. Probably any vasodilator would be effective, but many have unpleasant side-effects. The least unpleasant is nicotinic acid given in flushing doses. This may be 50–100 mg. given three times daily *before* meals. The patient must be warned that in 15–30 minutes a feeling of flushing, paraesthesiae, unpleasant fullness in the head, and an odd taste will be produced. These symptoms rarely last more than 15–20 minutes. If no great flush is produced when the nicotinic acid is taken by mouth, it may be given in doses of 50–100 mg. either intravenously or intramuscularly once daily. It is useful to continue this treatment for four to six weeks and then to discontinue it for about the same period before starting again. Nicotinic-acid derivatives which do not produce vasodilatation are not so beneficial.

Histamine in rising dosage has also been given, but it causes headache and perhaps is not so easy to control. If it is used, then a starting dose such as 0.1 mg. intravenously begins the course, and it can be increased by 0.1 mg. daily or even twice daily.

*Steroids.*—Like vasodilators, steroids may be very helpful in initiating a remission, but if no obvious effect is being produced within two or three weeks then they should be tailed off fairly quickly; but, if benefit is obtained, the steroids may be continued for two or three months. The usual careful watch for toxic results must be maintained. A good starting dose is 10 mg. of prednisone three times a day, and it may usefully be combined with nicotinic acid. A.C.T.H. in doses of 50 units daily by injection has also been prescribed for three or four weeks and then gradually reduced to a maintenance dose of 10 units daily for several months. The good effects are unfortunately transient.

*Arsenic.*—The vogue of arsenic therapy seems to have diminished recently, though there are many neurologists who still use it quite extensively. The usual mode of administration is to combine both organic and inorganic arsenic. In each course neoarsphenamine is given intravenously once a week in doses of 0.15 g., 0.3 g., 0.45 g., and 0.45 g. This four-weeks course can be repeated every three to four months. If the veins are difficult to enter, then intramuscular sulpharsphenamine in corresponding doses is given. Between injections liq. arsenicalis, 3–5 minims (0.2–0.3 ml.), is given for three weeks each month. Careful watch must be kept for intolerance to arsenic.

*Intrathecal Treatment.*—It has been suggested at Oxford that P.P.D. (purified protein derivative of tuberculin) given intrathecally produces a specific response in the cerebrospinal fluid of Mantoux-positive patients and that there may also be a helpful therapeutic effect. It is too early to assess the merits of this procedure, which can be carried out only in hospital.

Whichever of these means of treatment is used, if the patient's mobility is affected, whether owing to disturbance of power, tone, co-ordination, or sensation, then re-education with the help of trained physiotherapists is an essential part of treatment. It is probable that at present this may well be the most important part of treatment, and it is clear that this calls for special training of physiotherapists and for their being part of a team engaged specially in helping such disorders of mobility and equilibrium. Unless the therapists know what they are trying to achieve and have adequate leadership, they may well share the hopelessness that is so frequently seen in those faced with these patients. It is remarkable how much an enthusiastic doctor or department can achieve in restoring really useful function, quite apart from the help that can be given by introducing mechanical aids in the kitchen, bathroom, and elsewhere in the house.

## Symptomatic Treatment

In addition to treating the patient as a whole, some symptomatic treatment can give help.

*Hypertonus and Spasms.*—Occasionally hypertonicity is so great, especially in the hip adductors and plantar flexors,

that even with reasonable power walking is difficult. Some patients gain relief from meprobamate or mephenesin. The former can be started in 200-mg. doses three times a day after meals and the latter as mephenesin carbamate in 0.5-g. doses three times a day. Each can be pushed up to double or even treble these doses, provided the patient does not become too drowsy and there is no gastric irritation.

Extensor and flexor spasms may be very troublesome—disturbing rest and posture, and often being associated with a good deal of pain. Both meprobamate and mephenesin may help to diminish these contractions, but often so large a dose is necessary that the patient may be asleep the greater part of the day. In such a case it is probably better to give smaller doses such as 400 mg. of meprobamate three or four times a day and add small quantities of barbiturate such as phenobarbitone ½ gr. (32 mg.) or amylobarbitone ½ gr. (32 mg.) to each dose.

Unfortunately there are many advanced cases in which no drug treatment has any effect on the spasms, and life is rendered almost intolerable by the continuous violent and painful contractions. In such patients the only reasonable treatment is selective surgical section of peripheral nerves or fractional knock-out of spinal anterior nerve roots by means of phenol. Both these techniques require expert performance by someone familiar with the hazards of the procedures, but offer the possibility of turning an impossible existence into a more comfortable though paraplegic life.

*Vertigo.*—This symptom, with associated disequilibrium and vomiting, is usually due to a brain-stem plaque damaging the central connexion from the vestibular labyrinths. The treatment is the same as that of any acute vertigo. While vomiting is going on the intramuscular injection of 50 mg. of promethazine, chlorpromazine, or promazine will often ease the acute disturbance. If the attack is very severe the injection may have to be repeated some six hours later. The drowsiness which results is welcomed by the patient. Once the acute vomiting has ceased, then the same substances can be given by mouth in 25-mg. doses two or three times a day, or prochlorperazine ("stemetil") in doses of 5–10 mg. twice a day can be substituted. This drug produces less drowsiness.

*Sphincter Disturbances.*—The function of the bladder is commonly disturbed and the patient suffers from frequency, urgency, and precipitancy of micturition. Later incontinence may occur, but this is often due to a combination of precipitancy with diminished mobility. Retention is unusual except in the acute paraplegias due to a transverse plaque.

It is difficult to control the rapidly emptying spastic bladder except by sedation, but occasionally the use of a pill containing ergot 1 gr. (65 mg.) and ext. belladonnae sicc. ¼ gr. (16 mg.) may be helpful. Frequently, however, and especially in women, the urinary disturbance is accentuated by infection. If there is any real risk of this it may be helpful to keep the patient on small doses of sulphonamide such as sulphathiazole 0.5 g. twice a day, or sulphamethizole ("urolucosil") 0.2 g. twice a day for some months. If an obvious acute infection supervenes, then treatment with the specific substance to which the organism is sensitive is clearly indicated. Several courses may have to be given before the urine becomes sterile. Occasionally the long-continued use of sulphonamides may be interrupted with a course of hexamine mandelate, 0.5 g. three times a day for two or three weeks.

Retention of urine is treated by administering the stable esters of acetylcholine, of which there are many preparations available, in doses of 0.25 mg. intramuscularly or 1 mg. by mouth, repeated if need be. When this fails catheterization will be necessary.

The bowel difficulty is usually constipation, and diarrhoea and rectal urgency are most often the result of incautious aperients. It is safer to give only mild laxatives and supplement these by glycerin suppositories or "dulcolax" (2-(4:4'-diacetoxydiphenylmethyl) pyridine) suppositories. Enemas may be necessary, but it is essential to avoid irritating the bowel either from above or from below.

*Pain.*—This is a fairly frequent symptom in this disease. The pain may be associated with muscle spasms as already described, but other forms are as follows:

(*a*) Lightning pains.

(*b*) Root pain indistinguishable from a brachial neuralgia or sciatica or a trigeminal neuralgia.

(*c*) Headache due to plaques causing narrowing of the aqueduct of Sylvius and oedema, or interfering with the root entry zones of sensory nerves.

(*d*) Central pains due to involvement of the spinothalamic tract or the thalamus. Here the pain is of an intense burning and gnawing character, often with a profound affective reaction.

(*e*) Painful paraesthesiae.

The treatment of all forms of pain in this condition is to use the analgesics such as compounds of aspirin, phenacetin, and codeine in full doses unless gastric irritation and constipation are troublesome. Their efficiency is often greatly enhanced by adding small quantities of sedative such as amylobarbitone in doses of ½–1 gr. (32–65 mg.), and during the earlier part of the day by adding also an analeptic such as dexamphetamine 5 mg. This is particularly helpful for central pain and painful paraesthesiae.

*Pressure Sores.*—Once the patient is confined to a chair or bed the risk of pressure sores is great. This is particularly so if there is sensory impairment and urinary overflow.

They can be avoided only by scrupulous attention to the nursing care of the skin at the points of pressure, by changes of posture, and by the use of smooth bed linen or special seats. There is no drug which will help more than the efficient use of soap, spirit, and occasionally a silicone skin cream. The healing of pressure sores is so slow and the risk of spread in the paraplegic so great that treatment must be preventive. Once pressure sores are present, the only really effective treatment is prevention of weight bearing by the sore area. Necrotic tissue must be removed, and antiseptic creams may help to some extent.

## Morale

It must be clear now that a great deal can be done for these patients to provide some symptomatic relief, but it is equally clear that the essential part of treatment is the maintenance of morale in the patient and the relatives at as high a level as is possible. Patients can be helped by using all the benefits provided by the Health Service, in particular the provision of wheel-chairs, perhaps even motorized chairs, commodes, gadgets, and other appliances, but the most essential contribution to keeping up morale is the attitude of the medical staff of every kind who come into contact with the patient.

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Reporting on legal proceedings taken in 1957, the City Analyst for Birmingham writes in his Annual Report: "Only twice was it necessary to use the 'big stick' of prosecution, and on both occasions farmers were the culprits; the use of this weapon against food and drug retailers has to all intents and purposes been abandoned. A very different picture is presented in the first annual report made by me as city analyst in 1929; in that year 12 farmers were prosecuted in respect of 49 samples, and fines were imposed in 45 cases. Two of these farmers were each fined £100 for adulteration on the grand scale, which it was calculated resulted in both cases in the sale of 100 gallons of water per week as milk. In addition, summonses were issued in respect of four other foods and drugs. The total fines paid by offenders amounted to £328: this figure is practically ten times as great as the corresponding one for 1957, and this reduction of 90% is an indication both of a greater sense of responsibility on the part of manufacturers and of a changed attitude on the part of local authorities."

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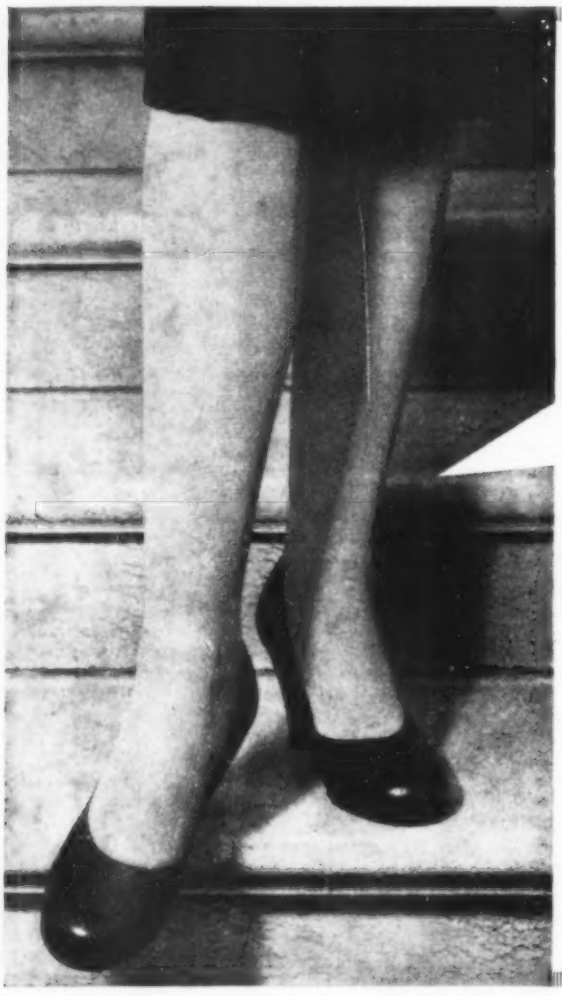

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# FIRST B.M.A. ANNUAL CLINICAL MEETING SOUTHAMPTON, DECEMBER 4-7

When Professor A. P. THOMSON, President of the British Medical Association, formally declared open the Association's First Annual Clinical Meeting, in the Guildhall at Southampton at 10.30 a.m. on Friday, December 5, the meeting was in fact already well under way. Some two hundred doctors, many from far beyond the Southampton region, had attended with their wives and guests a civic reception the previous evening; and two panel discussions —on "Hand Injuries" and on "The Treatment and Prevention of Deafness"—had already taken place.

### A Change of Emphasis

The President, after expressing the meeting's gratitude to the Mayor and Corporation of Southampton for putting their fine Guildhall at the Association's disposal, referred to a remark made by the chairman of the Southampton Division the night before. Dr. R. S. Russell-Smith had said that they in Southampton had spent a great deal of time in preparing for this first Annual Clinical Meeting of the B.M.A. with but one hope in mind: that the meeting might prove a serious contribution to a change of emphasis in the Association's work. It had been feared in Southampton, said the President, that in the meetings organized by the B.M.A. the cultivation of professional excellence had been neglected in the press of political events. With Southampton's hope that the emphasis on professional work would be restored Professor Thomson said he wished to identify himself completely. He hoped that this first Clinical Meeting would be the first of many.

At the reception the previous evening in the Guildhall, given by the Mayor and Corporation, the Mayor, Alderman R. R. H. HAMMOND, in his welcome to the delegates said that Southampton was proud to have been chosen for the first B.M.A. Annual Clinical Meeting. Dr. R. S. RUSSELL-SMITH likened the occasion to the birth of a baby—always an exciting event. The B.M.A. was not just a medico-political organization, he said. The meeting showed that the Association had a real interest in clinical medicine. He thanked particularly Dr. J. G. McDowell and Dr. R. P. W. Shackleton, respectively honorary general secretary and honorary science secretary, for their untiring work in preparing for the meeting.

## PANEL DISCUSSIONS

*Friday, December 5, 9.30 a.m.*

### Hand Injuries

Between 50 and 70 people attended each of the two simultaneous panel discussions held at 9.30 a.m. on Friday morning. In the one on "Hand Injuries," with Mr. J. N. BARRON (Salisbury) in the chair, Mr. L. W. PLEWES, of Luton, and Mr. R. G. PULVERTAFT, of Derby, answered questions on many aspects of this subject—which, as the chairman stressed, is of such great importance to the general practitioner. The panel first considered the organization of a hospital department for dealing with hand infections. Mr. PLEWES said only one thing counted: "to have a person who is interested in hand infection and to let him have his head—one permanent member of the staff, not a bird of passage."

### Treatment of Infections

The whole treatment of hand infections had changed with the advent of antibiotics, said Mr. PULVERTAFT. "We don't see the pulp infection that we did; it is more often the minor hand infections we see now; the major ones are scotched very rapidly." Dr. N. B. EASTWOOD (Oulton Broad, Suffolk) said treatment was made more difficult by patients going on working until it was too late. Mr. PLEWES, however, took up Mr. Pulvertaft's remark about antibiotics. He believed that we used them too much. There were only two indications for antibiotics in hand infections, he said—cellulitis or a spreading lymphangitis. Penicillin should not be given for pulp infections, paronychia, and so on. Challenged by Dr. W. R. S. CAMPBELL (Oxford) for his reasons for saying this, Mr. PLEWES said, first, there was the presence of increasing numbers of insensitive staphylococci; in some hospitals the incidence was now in the region of 80%. There was no logic in giving these patients penicillin—"after all, it is the only safe antibiotic we have got, isn't it?" Secondly, one should rely on the most effective treatment, which in his view was not antibiotics. 98% of infections in the hand were due to *Staph. aureus*, which caused its damage by its exotoxins producing tissue necrosis. "Operate on these patients and remove the necrotic tissue; that is the only thing that is important." The incision should be made directly over the pus, not by the standard incisions, under either general or local anaesthesia. The main thing was to have a tourniquet and an assistant. Dr. J. A. SADLER (Cambridge) objected that in general practice patients expected penicillin as a routine. The treatment was by immobilization of the hand and antibiotics. "We don't find so many resistant staphylococci as you talk about in hospital." The patients did very well indeed. Mr. PLEWES endorsed the importance of immobilization and mentioned that in his view any form of heat was harmful. Dressings for hand injuries could be minimal if the slough had been removed at operation: not a lot of gauze and wool which crippled the patient, but just a small strip dressing to keep the skin edges together. "We do a lot of damage to our patients by wrapping them up in cotton-wool. We ought to aim at getting our pulp infections back to work within one and a half days, acute paronychias back to work in 24 hours, acute suppurative tenosynovitis within three days." There was no place for operative treatment in acute suppurative tenosynovitis, where there was a lovely closed space capable of holding a hundred times enough penicillin to kill any organism. All that was needed was to put a needle into the space, aspirate the few drops of pus which were there, inject 500 units of penicillin, the patient was cured.

### Cut Tendons and Mallet Finger

The problem of severed tendons was discussed by Mr. PULVERTAFT. Dealing first with the extensor tendons, he described the treatment of lesions at various levels. Lesions over the proximal phalanx would recover if the finger was splinted in full extension. At the back of the hand primary suture was necessary. Division of the flexor profundus beyond the level of the sublimis attachment at wrist and palm level might be treated by primary suture; but if the tendons were divided between the distal palm-creases and the insertion of sublimis, where there was a rigid fibrous sheath, primary suture was unwise. The correct treatment then was suture of the skin only, so that later the tendons could be replaced by a free tendon graft taken from some other part of the body. Mr. J. S. ELLIS (Southampton) asked if there was any place for secondary suture in the no-man's-land of fibrous tissue. As a general policy, Mr. PULVERTAFT thought there was not. Replying to Dr. M. B. CARSON (Southampton), he said that a finger would work almost as well with a profundus tendon alone as with both profundus and sublimis tendons.

Mr. PLEWES expressed definite views on mallet fingers. Instead of the disabling plasters with the finger held in the flexed position, he used a tiny splint of "perspex" over the distal two-thirds of the finger, leaving the proximal joint free. The patient could return to work wearing the splint, which he kept on for six weeks, thereafter wearing it only

at night. There was no place for surgery in this condition. Mr. PULVERTAFT used a "pin" beneath the skin, but confessed to less than 90% cure. Sometimes he performed open surgery on these cases. Mr. J. B. SHIELD (Fordingbridge, Hants) found that patients often came for advice three or four weeks after injury, and he felt that it was asking too much to expect a response to splinting alone in such cases, but Mr. PLEWES claimed 45% cures in patients seen after six weeks.

### Fractures and Crush Injuries

Mr. PULVERTAFT felt that there should be a complete reorientation of our ideas on hand fractures. Many of these would do better by mobilization and pinning at an open operation. He admitted that this required most careful and time-consuming surgery, but, if this was the best way of treating them, it should be done. Mr. PLEWES agreed that some fractures must be operated upon. He did not agree with the statement in two recent textbooks that there was no reason for splinting fractures of the hand. One fracture—the impacted neck of the fifth metacarpal—could be left without splinting. "If we don't do something to our patients to relieve the pain they are not going to use the hand." In answer to Mr. ELLIS, who put in a plea for the functional treatment of fractures of the metacarpals, Mr. PLEWES thought that these were often over-treated. He thought 14 days was usually long enough in plaster.

Mr. BARRON remarked that all injuries except burns were caused by cuts or crushes. In severe crush injuries, Mr. PLEWES said, only one thing mattered, and that was the prevention of further injury by oedema to the structures that had already been damaged. He recommended delayed treatment with refrigeration and elevation. Mr. PULVERTAFT agreed that the prevention of oedema was most important, but believed that elevation was the best method of treatment. In reply to a question from the floor, he said that the correct first aid for a dirty crush-injury was to do nothing to the hand: "Put a dressing on, but *don't clean* it, don't put on antiseptics; let the hospital deal with the cleaning under anaesthesia." The best cleaning of a wound was by washing, washing, and washing.

### Treatment and Prevention of Deafness

The importance of careful clinical observation in the diagnosis of deafness, both in the very young and in the elderly, was emphasized by the panel, consisting of Miss EDITH WHETNALL (London) and Mr. F. MCGUCKIN (Newcastle upon Tyne), which discussed "The Treatment and Prevention of Deafness," under the chairmanship of Mr. N. W. MACKEITH (Southampton). Replying to a question from Dr. R. S. RUSSELL-SMITH (Southampton), Miss WHETNALL stressed the importance of diagnosing deafness in children very early. Usually by three months a child could suppress undesirable noises and would react appropriately to meaningful sounds, and by six months he should begin to imitate his mother's voice. Deafness might be detected by observing the failure of a child to react like this, although other causes such as prematurity, mental deficiency, or simple neglect must be considered. To test the diagnosis sound must be brought to the baby by means of a hearing-aid—even very small babies could wear an aid. A deaf baby must wear its aid continuously so that he could learn to appreciate sounds in the same way as would a normal baby. The longer he was deprived of sounds, the more difficult would it be for him to learn to hear and later to talk. Thus early diagnosis was the keystone of successful treatment. The management of these children must of course be carried out through the mother, and it was important to explain to her that dramatic and immediate results could not be expected. Mr. MCGUCKIN made the point that surgical treatment was available only for middle-ear types of deafness, which were uncommon in the very young.

Dr. D. M. T. GAIRDNER (Cambridge) asked the panel what the lesion was in deafness following purulent meningitis and what was known of the pathology of congenital deafness. Mr. MCGUCKIN pointed out that the perilymph was continuous with the subarachnoid fluid, and that, unless it became sealed off early in the disease, infection from the meninges might spread to the inner ear, causing deafness and vestibular symptoms. If only one inner ear was damaged the deafness was unlikely to be detected in early childhood. Miss WHETNALL divided cases of congenital deafness into those arising from hereditary factors, those associated with maternal illness in pregnancy, and those resulting from disorders during or immediately after birth. There might be any degree of involvement, from the complete absence of the cochlea to the loss of only a few of the organs of Corti. In those cases due to maternal rubella it was only the organs of Corti that were affected. These children were often extremely intolerant of noise, and this fact might render the wearing of an unsuitable aid most uncomfortable.

Dr. MARY CAPES (Southampton) asked the panel whether they thought that cases of partial deafness in children were being missed, thus giving rise to educational difficulties when the child arrived at school, where the true reason might not be appreciated. How far was screening advisable? Mr. MCGUCKIN replied that an audiogram was no more valuable than an *x*-ray; it was merely part of the clinical investigation. The patient's performance on testing would depend on many factors, including the speed of onset of the deafness. "Machines can go wrong," he said, and the shrewd clinician should be able to predict the audiogram result. Miss WHETNALL agreed, and thought that we were becoming too reliant on machines. Careful clinical assessment was every bit as scientific as audiology. The CHAIRMAN summed up by saying that it seemed that the audiogram was a good servant but a bad master.

### Deafness in the Elderly

Dr. JOHN L. STRUTHERS (Southampton) asked the panel what the indications were for referring older patients with increasing deafness to a specialist. Mr. MCGUCKIN said that they came to a doctor because they or their relatives felt they were losing contact with others. The common cause of deafness over the age of 55 or 60 was cochlear degeneration. These patients had difficulty in hearing consonants. As well as the straightforward difficulty in hearing sounds, the normal damping effect on undesirable noise was lost and the patient tended to get words jumbled up, particularly if speech was fast. The provision of a hearing-aid of limited output, combined with instructions to the household to speak slowly and distinctly, was all that was required. The CHAIRMAN, while agreeing, thought that without a trial it was very difficult to tell how much a hearing-aid would help. The old-fashioned speaking-tube was often very useful, he added.

In reply to a question from Dr. W. H. N. ANGUS (Southampton) on modern surgical techniques for the relief of deafness Mr. MCGUCKIN said that only middle-ear deafness was amenable. There were two main problems—otosclerosis and the late effects of otitis media. In the former condition the underlying lesion was the ossification of the elastic membrane around the oval window. In a few cases it was possible to fracture this new bony tissue during the inactive stage, thus mobilizing the stapes with excellent results. In the fenestration operation the oval window and the ossicles were abandoned and a new hole was made into the external semicircular canal. This would give the patient an adequate degree of hearing. In chronic otitis media the contents of the middle ear except for the stapes had been lost. Various operations had been devised to re-form the middle-ear chamber by skin-grafting, the essential requirement being the presence of some healthy mucous membrane in the region of the round window. The results of these operations could be very satisfactory, with a hearing loss of only ten to fifteen decibels. In answer to a question about their percentage success, Mr. MCGUCKIN stated that he preferred to regard them as salvage operations. In his opinion about half the patients could be so salvaged.

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* *Comptes rend. Soc. de Biol.*, 1948, **142**, 819.

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Dr. RUSSELL-SMITH (Southampton) asked the panel for their opinion on the dangers of treating acute otitis media with penicillin or sulphonamides. The CHAIRMAN felt that this was a matter of fine clinical judgment. If there was an appreciable amount of pus in the middle ear, then the drum should be incised, but early cases could be safely treated by medical means alone. Both the other members of the panel agreed.

## FIRST GENERAL SESSION

*Friday, December 5, 10.45 a.m.*

### Operative Treatment of Duodenal Ulcer

Dr. H. C. MAURICE WILLIAMS (Southampton) was chairman for the first general session, which he introduced.

Professor JOHN BRUCE (Edinburgh), P.R.C.S.Ed., spoke on the choice of operation for duodenal ulcer. He emphasized that the surgeon could now approach his patient with a view to providing the most suitable type of operation, and this should be assessed beforehand by a maximal histamine test meal (Kay's), in order that the hazards of further ulceration could be avoided. Professor Bruce described the two forms of operation in vogue as being those attacking the gastric secretion by interruption of the nervous pathway accompanied by some form of "drainage operation," and those that reduced the degree of acidity by removal of secreting gastric tissue. He demonstrated that the reduction might be measured by Kay's test and also from an academic point of view by counting the acid-secreting cells. He showed that there was a correlation between their number and the concentration of acid as measured.

He divided the cases into three groups as determined by their capacity to produce various concentrations of acid. One-third would show less than 30 mEq, and these should therefore respond to gastro-enterostomy with vagotomy. The second group was those with medium secretion of acid, and these should be treated by partial gastrectomy of standard type. There remained some 17% who were high acid-secretors, above 50 mEq, and these would need a radical gastrectomy with vagotomy.

The results of these operations could be predicted, especially if the maximal histamine test meal was repeated. Only those showing a high acidity at the post-operative test would be liable to further ulceration, either of the suture line or of the jejunum. He concluded by answering many questions.

### Prevention of Reactions to Antibiotics

Professor L. P. GARROD (London) discussed reactions to antibiotics, dividing these into three types—those causing sensitivity reactions or direct toxicity to various organs and those associated with superinfection. He pointed out that direct toxicity usually was related only to a few specialized tissues such as the kidneys, marrow, and the eighth nerve.

Chloramphenicol was a drug which should be reserved for serious indications—namely, whooping-cough in infancy, typhoid fever, and certain virus infections. Penicillin was apt to cause sensitivity reactions, and these might be severe and of the anaphylactic type, or more akin to serum sickness. He pointed out the doubtful value of skin tests, especially as a precaution against the more serious forms of reaction. The occurrence and significance of antibodies to penicillin in the blood needed further study.

The tetracycline group, or combinations of antibiotics with a similar "broad" effect, were apt to result in superinfection of the mouth, gastro-intestinal tract, or bronchi with yeasts or the overgrowth of resistant coliform, *Proteus*, and *Pseudomonas* species. He also stressed the more serious invasion by antibiotic-resistant staphylococci, especially after gastro-intestinal surgery. He thought the use of tetracycline preparations unwise after partial gastrectomy in cases where the gastro-intestinal flora might previously have been disturbed by long-acting sulphonamides, with suppression of the normal flora.

### Sudden Death in Infancy

Dr. D. M. T. GAIRDNER (Cambridge) concluded the session with a discussion on sudden death in infancy, his figures being based on the first 81 cases from an inquiry by a combined team in Cambridge and London. If their figures were applied to England and Wales some 1,600 such deaths might be occurring annually. Sudden and unexpected death accounted for one-quarter of all deaths in the age group 2 weeks to 2 years. Most babies died in the colder months, and this ratio was similar in Australia. There was also a differential between the sexes, and infections, however trivial, appeared to be involved. Dr. Gairdner showed histological sections demonstrating that infections of the respiratory tract were especially important. Although full post-mortem examinations had been made on all their cases, there was a large number where no satisfactory medical cause for death was found. Post-mortem evidence did, however, show that many of these cases were not due to asphyxia.

## SECOND GENERAL SESSION

*Friday, December 5, 2.15 p.m.*

The chairman at the afternoon general session was Dr. S. WAND (Birmingham), and the three invited speakers were Dr. A. RAE GILCHRIST, P.R.C.P.Ed., Professor A. M. CLAYE, P.R.C.O.G., and Dr. NEVILLE OSWALD.

### Diagnosis of Acute Myocardial Infarction

Dr. A. RAE GILCHRIST (Edinburgh) said that the typical classical picture of acute myocardial infarction was often over-emphasized. Clinically the condition might present in various ways. There were (*a*) the painful syndromes which were associated with shock and collapse; (*b*) the cases in which the sudden onset of dyspnoea predominated; (*c*) those in which weakness, collapse, or even coma was the presenting symptom, or in which a sudden unexplained cerebrovascular incident occurred, or where the patient failed to improve as expected after surgery or an acute haematemesis; (*d*) sudden embolic phenomena which should suggest the possibility of an infarction; (*e*) changes of rhythm, notably auricular fibrillation and heart block in the middle-aged and elderly; and, lastly, (*f*) restlessness in an elderly patient without obvious cause.

In making the clinical diagnosis, more weight should be put on the abruptness of the onset rather than the duration or the severity of the illness. The diagnosis was established by the rapid development of signs of tissue destruction—leucocytosis, fever, elevated serum transaminase—and subsequently by an increased sedimentation rate. An E.C.G. was 95% accurate, given good interpretation, and was also valuable in assessing healing.

Comparing the accuracy of clinical as against post-mortem diagnosis, Dr. Gilchrist said that in a hospital series the diagnosis was almost as often wrong (37%) as right (43%), while in 20% the diagnosis was overlooked and only revealed post mortem. The errors of diagnosis included gross coronary atheroma with occasional local occlusions without infarction, pulmonary embolism, pneumonia, and post-operative collapse. The last occurring within three or four days of operation should always suggest acute myocardial infarction. Correct diagnosis was important, as it might make it possible to prevent embolic phenomena, the increase of shock, or congestive failure.

After his address Dr. Gilchrist answered questions. In reply to one on the value of the serum transaminase estimation, he said it could be of considerable use in the first three or four days. It reached a maximum within 48 hours, immediately preceding the rise in E.S.R. Though not as good as skilled reading of an E.C.G., it could be helpful. Asked about the indications for anticoagulant therapy, he said it was indicated in virtually all cases except those with advanced liver disease, renal insufficiency, a recent history of peptic ulcer, or severe anaemia. Were anticoagulants going out of fashion? They should be out

of fashion, said Dr. Gilchrist, if there was no reliable laboratory control. Anticoagulant therapy protected patients against embolic phenomena, particularly pulmonary emboli ; any patient who had a pulmonary embolism within two or three weeks of coronary infarction was in very grave danger.

Asked if the E.C.G. was sometimes negative soon after infarction and positive a few days later, Dr. Gilchrist said the time when it became positive varied. In most people it became positive in 12–24 hours, in others it might take 10–72 days. In doubtful cases a series of E.C.G.s should be taken at two- to three-day intervals. Replying to a question about the value of corn-oil emulsion, he pointed out that it was a vegetable oil which in fact did reduce the blood cholesterol. The blood cholesterol was high in the younger age groups, but no one had shown that its reduction reduced the degree of atheroma.

### Prevention of Severe Pregnancy Toxaemia

In the last 25 years, said Professor A. M. CLAYE (Leeds), the causes of maternal mortality had altered greatly in their order of frequency. "Eclampsia and other toxaemias" had now replaced puerperal sepsis as the commonest cause. He quoted mortality figures for 1955 in which 112 deaths had been due to toxaemia, 68 to abortion, and 41 to post-partum haemorrhage. In about half the deaths from toxaemia the antenatal supervision had been inadequate, the responsibility for this being divided between patients and their attendants. Patients who frequently defaulted from antenatal clinics had an increased incidence of toxaemia.

Dixon Hughes, of Sydney, had said that, if the mother did not gain more than 8 lb. (3.6 kg.) between the 20th and 30th weeks, she was unlikely to get toxaemia ; if more than 8 lb. then it was much more possible. Toxaemia was commonest in first pregnancies. In those who had previously had toxaemia the chances were fifty-fifty, but once a woman had had toxaemia she should attend hospital for her subsequent pregnancies. The patients who were prone to develop toxaemia were those with twins, diabetics, and those in whom the blood pressure was more than 140/90 at least twice before the 20th week. Where there was no previous essential hypertension, 1.8% developed toxaemia, but in those with a previous history 35.5% developed it. In about half the women with essential hypertension the blood pressure fell to normal in the second trimester, and therefore the condition might be missed if they first attended during that time. Professor Claye described how to get a clean specimen of urine uncontaminated by vaginal discharge, and reminded his hearers that albuminuria might be due to urinary infection or chronic nephritis. When albumin was found in pre-eclamptic toxaemia it was a late sign, while headache, vomiting, and epigastric pain were very late signs.

The patient with toxaemia might lose her baby, develop eclampsia, or have an accidental haemorrhage. Describing the routine hospital treatment of toxaemia, Professor Claye said that the use of diuretics and hypotensive drugs was not yet established. Once albuminuria had appeared it rarely cleared up until after parturition, and even then it might continue for up to two years. The response of the blood pressure varied considerably. Regarding termination of pregnancy, there was little hesitation after 36 weeks ; between 32 and 36 weeks he tried to tide the patient over unless her condition was deteriorating. If severe toxaemia developed before the 32nd week, the baby had little chance of survival either way. Caesarean section might have to be performed in a fulminating case.

Professor Claye then answered some questions.

### Management of the Pulmonary Complications of Influenza

DR. NEVILLE OSWALD (London) described the pulmonary complications seen during the Asian influenza epidemic in October, 1957. He said that reports showed that 5% of the cases developed pneumonia or other complications. He deprecated the routine use of antibiotics for influenza ; most of the pneumonias had been straightforward. The influenzal virus was apt to pave the way for bacterial infection of the respiratory tract which might lead to tracheobronchitis, oedema, pneumonia, or toxaemia. The tracheobronchitis might lead to severe obstruction with stridor and indrawing of the soft tissues of the neck during inspiration. If antibiotics failed to overcome the obstruction rapidly, intrabronchial intubation might be life-saving. Tracheotomy with suction was the method of choice, but bronchoscopy was permissible in extreme cases. In the lungs, oedema might be widespread before pneumonia developed ; it could be relieved to some extent by aspiration through a tracheotomy tube.

The bacteriology of pneumonia complicating influenza did not differ materially from that of ordinary pneumonia, except that perhaps staphylococcal superinfection might be rather commoner. The great majority of pneumonias responded to adequate doses of penicillin or one of the tetracycline group. About half the staphylococcal cases responded equally well to these drugs, but the remainder were caused by resistant strains. Hence sensitivity tests, which took 24 hours to perform, were most important in staphylococcal pneumonia. If the results of the tests could not be awaited, intravenous erythromycin was most likely to be effective, given in doses of up to 1 g. four-hourly for the first day or so. The severe toxaemia might lead to peripheral circulatory failure, which might be fatal in a few hours. Intravenous hydrocortisone, 100 mg. six-hourly, in a drip, together with antibiotics, might prevent the fatal collapse. Lung abscess was seen as a late complication, and it responded well to antibiotics.

Asked if staphylococcal and convalescent sera were of any use in these overwhelming cases, Dr. Oswald replied that, though they were used, it was difficult to assess their value, as so many drugs were employed with them. "If you have it, use it," he said. If oxygen was needed, a tent was best for a young child and a mask or spectacles for adults. He advised a rate of 5–6 litres a minute.

## TELEVISION AND FILMS

For many, one of the major attractions of the meeting, because unrealizable with the resources at the disposal of most local medical societies, were the two "live" colour television programmes of operations from the Southampton General Hospital and the "Transatlantic Clinical Conference." These admirable contributions were sponsored by Smith Kline & French Laboratories, who for the colour television were using their own experimental mobile van and equipment.

### Voices Across the Atlantic

The British and the American Medical Associations joined together for an hour's clinico-pathological conference on Friday afternoon, at which two cardio-pulmonary cases were discussed blind by picked teams on either side of the Atlantic. The link was by transatlantic cable, and the voices of the speakers were transmitted by loudspeakers to each audience. This medical brains trust—which certainly enthralled the large audience in Southampton Guildhall—went as follows: Each side had beforehand been given a written case history summarizing the clinical findings, investigations, and course of the case to be diagnosed, together with slides of relevant *x*-ray films, E.C.G.s, etc. The highlights of the case were then recapitulated over the transatlantic telephone by the physician presenting it, after which he answered questions from the opposing panel, whose task it was to make a diagnosis. Finally, he gave the answer, as found at necropsy, over the telephone cable for all to hear.

The British team in the Guildhall at Southampton were Dr. W. D. BRINTON (Winchester), the moderator and organizer of the programme, Professor JOHN MCMICHAEL (London), Dr. J. G. SCADDING (London), and Mr. T. HOLMES SELLORS (London). Opposing, at the A.M.A. Clinical Meeting in Minneapolis, were Dr. JAMES R. FOX (Minneapolis), as moderator, with Dr. JOHN BRIGGS (Saint Paul) and Colonel JAMES A. WEIR (FitzSimmons Army Hospital). For the

benefit of the two audiences watching the programme enormous photographs of the members of the opposing team were mounted on the stage, and when one of them spoke a red light went on over his picture.

The British team bowled first, and the ball they sent the Americans most certainly was a "fizzer." Professor McMICHAEL described the case of a man in his fifties with a progressive and eventually fatal pulmonary hypertension who had first presented some three years earlier with a mild febrile illness, loss of energy, a normochromic anaemia, and an E.S.R. of 85 mm. After a remittent but progressive course during which there developed a transient attack of blindness, dizziness, and an idiopathic hyperglobulinaemia, the patient died in right heart failure. The answer, which not surprisingly floored both the teams, was a myxoma of the left atrium obstructing the blood flow. The American case, ably presented by Dr. FOX, though involving a triple diagnosis, was by comparison straightforward. The correct diagnosis of silicosis, pulmonary tuberculosis, and as the final event a bronchial carcinoma with widespread pulmonary metastases was successfully made for the British team by Dr. SCADDING.

There was no doubt that the British audience found this first transatlantic clinico-pathological conference between B.M.A. and A.M.A. teams very good fun and highly instructive. The American team's voices reached the Guildhall perfectly clearly.

### Colour Television

Those who have attended recent B.M.A. Annual Meetings will be familiar with the pattern of the Smith Kline & French Laboratories' colour television demonstrations of surgical operations. The cameras divide their attention between the operation itself, which is telecast as it proceeds, and a panel of experts in a temporary studio at the hospital who demonstrate charts, *x*-ray pictures, etc., and answer questions relayed from the audience in the meeting hall. On both Friday and Saturday, operations from the Southampton General Hospital were televised during the lunch hour to the audience in the Guildhall. The moderator on both days was Mr. H. H. LANGSTON (Winchester).

On Friday two operations were shown. The first was the repair of an atrial septal defect under hypothermia, in which the surgeon was Mr. E. F. CHIN and the anaesthetist Dr. E. S. MACHELL. The studio panel who answered questions on the case were Dr. R. V. GIBSON (London), Dr. D. J PEARCE (Southampton), and Mr. I. K. R. McMILLAN (Southampton). The second was an operation for lymphoedema, where the surgeon was Mr. J. E. LAING and the anaesthetist Dr. P. J. HORSEY. Mr. J. N. BARRON (Salisbury) answered questions in the studio. On Saturday the first operation was a partial thyroidectomy for a "cold" nodule by Mr. G. ST. J. HALLETT (anaesthetist, Dr. H. C. J. BALL), and in the studio were Mr. T. ROWNTREE and Dr. H. K. MELLER (both of Southampton). Next was shown an arthrodesis of the knee for advanced osteoarthritis by Mr. D. E. MACRAE (anaesthetist, Dr. C. B. PICKEN), with Mr. J. S. ELLIS and Dr. J. PRESTON, of Southampton, answering questions. Finally Mr. L. A. RICHARDSON performed a stripping operation for varicose veins (anaesthetist, Dr. W. L. M. BIGBY), with Mr. ROWNTREE in the studio.

### Medical Films

Dr. R. P. LISTON, chairman of the B.M.A. Film Committee, compèred the showing of three films from the B.M.A. Film Library, for an hour on Friday evening. All were in colour and sound. The first on "The Jugular Venous Pulse," made by the Wellcome Film Unit, had as its commentator Dr. PAUL WOOD. It illustrated modern instrumental techniques for analysing the jugular pulse. In the second film, "The Management of Twins in Pregnancy and Labour," produced by the Wellcome Foundation Ltd., the medical authority was Professor W. C. W. NIXON. The last film was on "The Treatment of Cardiac Arrest." It had been made by the Department of Medical Illustration, Guy's Hospital Medical School, under Sir RUSSELL BROCK's direction. The film showed emergency exposure of the heart and cardiac massage in a case of cardiac arrest, and also demonstrated the use of the defibrillator.

### DINNER AND RECEPTION

On the Saturday evening a dinner, attended by nearly 200, was held in the Royal Pier Pavilion. Speeches were made by the BISHOP OF SOUTHAMPTON, who proposed the toast of the British Medical Association, to which the President, Professor A. P. THOMSON, replied. "The Guests" was proposed by Dr. D. P. STEVENSON, Secretary of the Association, and the Vice-Chancellor of Southampton, Dr. D. G. JAMES, replied. Professor THOMSON said that since becoming President of the B.M.A. he had put to himself anxiously the question, What were the Association's purposes? Medicine had passed through three revolutions and it was still in process of adjusting itself to the last of them, which, stemming from the philosophies of men such as Herbert Spencer, held that the doctor had a duty not only to the individual but to society as a whole. That accounted for the perhaps undue concern over politics in the recent past, and he therefore welcomed a meeting devoted entirely to clinical medicine. It was a return to the original idea that what really mattered in medicine was the quality of the people practising it. The other two revolutions medicine had experienced in the past, and only slowly digested, had been the Hippocratic revolution through which medicine became rational and the ethical concept was introduced, and the scientific revolution beginning in the sixteenth century which had established experiment as the test of truth—and the implications of this latter revolution had taken over 300 years to be fully absorbed.

The night before, the Southampton Division of the B.M.A. gave a most successful informal reception at the Palm Court Restaurant, at which Dr. and Mrs. R. S. RUSSELL-SMITH received the guests.

In all, 325 doctors registered for this first B.M.A. Annual Clinical Meeting. On all sides it was accounted to have been a great success. Reports of the panel discussions, the final general session, and the visits to local hospitals for clinical demonstrations on the Saturday, and of the Sunday morning outings, will be given next week.

# Nova et Vetera

### RICHARD BRIGHT

Reference was made in the *Journal* last week (pp. 1402, 1422) to the commemoration of the centenary of Richard Bright's death, which occurred on December 16, 1858. Today he is remembered chiefly for his description of the disease to which his name has been given, and through the passage of time his many contributions on other subjects and his wide interests and accomplishments have been largely forgotten.

Bright was born in Bristol on September 28, 1789, and in 1808 began the study of medicine at Edinburgh. Two years later, while still a student, he accompanied Sir George Steuart Mackenzie and (Sir) Henry Holland on a two months' tour of Iceland, and contributed chapters on botany and zoology to Mackenzie's account of the expedition (*Travels in Iceland*, 1811).

On his return, Bright studied for a time at the united hospitals of Guy's and St. Thomas's, and graduated M.D. Edinburgh in 1813. In the summer of 1814 he embarked on a lengthy Continental tour, which included Belgium, Holland, Germany (where he spent some time at the Charité in Berlin), and Austria. In the spring of 1815 he travelled through lower Hungary and published an excellent description of the social and economic life of that country (*Travels from Vienna through Lower Hungary*, 1818). Some account of this little-known volume of over 700 pages was given in this *Journal* by R. T. Williamson[1] over thirty years

ago. It exemplified "Bright's wonderful power of observation and description, his wide reading, his accuracy, as is shown by the tables, maps and appendices, and his artistic ability, for it is illustrated by beautiful engravings from sketches by himself."[2]

Returning to London, Bright was appointed assistant physician to Guy's Hospital in 1820, and full physician in 1824, resigning in 1843. He was elected F.R.C.P. in 1832, and, on the accession of Queen Victoria in 1837, was appointed her Physician Extraordinary. His first description of chronic nephritis was given in vol. 1 of his *Reports of Medical Cases*, 1827, and a more extensive account appeared in *Guy's Hospital Reports* in 1836. Sir William Hale-White[3] has published a description of these writings, including a condensed version of the 1836 paper; they have also been reprinted under the editorship of A. A. Osman.[3] Vol. 2 of the *Reports of Medical Cases* appeared in two parts in 1831. It is devoted to diseases of the brain and nervous system.

Hale-White[4] has also reminded us of Bright's important writings on subjects other than renal disease. These include spastic paraplegia, epilepsy, localization of cerebral function, aphasia, glycosuria and pancreatic disease, cirrhosis of the liver, acute yellow atrophy, diaphragmatic hernia, chronic peritonitis, Addison's disease, appendicitis, the administration of oxygen, heart block, and the lungs in whooping-cough. His description of unilateral (Jacksonian) epilepsy preceded the more important account given by Hughlings Jackson in 1863. He was the first to describe Addison's disease, but he did not connect the symptoms with disease of the adrenals. In 1836–9 he collaborated with Thomas Addison in writing *Elements of the Practice of Medicine*, vol. 1. No second volume appeared, and the first, now a rarity, contains what is probably the first accurate account of appendicitis.

Bright's death, which occurred at his house in Savile Row, was due to aortic disease. He was twice married. His first wife was the daughter of William Babington, M.D., another illustrious physician of Guy's Hospital.

The portrait of Bright was supplied by the Wellcome Historical Medical Library.


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2 Hale-White, W., *Guy's Hosp. Rep.*, 1921, **71**, 1.
3 *Original Papers of Richard Bright on Renal Disease*. Edited by A. A. Osman. 1937. Humphrey Milford, London.
4 Hale-White, W., *Guy's Hosp. Rep.*, 1921, **71**, 143.


The 43rd Annual Report of St. Dunstan's for the year ended March 31, 1958, is entitled "Wars end—but blindness remains. . . ." The report is divided into three sections, "Learning to be blind," "Out into the world," and "Their future is bright." The oldest member of St. Dunstan's is now 90 years old; he lost his sight during an incendiary bomb raid in the second world war. "Since the last shot was fired in World War II," says the report, "we have received no less than a further 500 young men. Some were certainly casualties in Korea, Kenya, and Malaya, but the majority have been men whose sight for one reason or another failed from old wounds, the results of privation and hardship suffered in P.O.W. camps, jungle fever and tuberculosis, or from illnesses contracted on war service."

# Reports of Societies

## RESULTS OF LEUCOTOMY

[FROM A SPECIAL CORRESPONDENT]

The Section of Neurology of the Royal Society of Medicine took a look, on November 6, at the results of leucotomy in the light of recent long-term follow-up studies. In addition two neurosurgeons described, respectively, their experience of a modified rostral leucotomy and of orbital undercutting.

### In Depression

Dr. ALICK ELITHORN said he had followed up, by clinical assessment and questionary to patient and relative, some 105 patients under Dr. Eliot Slater's care who underwent leucotomy at Queen Square before 1954. He had paid particular attention to the effects of the operation in depressive illness, and his findings supported the thesis, recently rejected by Garmany,* that there are two distinctive types of depressive illness, one a reactive depression determined by environmental factors and the other the so-called endogenous depression which is determined at least partly by one or two genes of large effect. Using the customary criteria, Dr. Elithorn had separated the possible "endogenous depressions" from the other types and compared them in terms of response to leucotomy. It was clear that the results were very much better with the endogenous patients and that these patients were much more enthusiastic about the operation than were those with reactive depression: of the endogenous depressives, 84% were glad to have had the operation and only 1 out of 32 regretted it; while, of the reactive depressives, 51% were glad to have had the operation and 8 out of 35 regretted it. These results were not attributable to the type of operation carried out: in the series 50 had the standard and 55 the modified procedure.

Within the group of reactive depressions the outcome varied according to the kind of environmental determinant. Thus the results were very much worse where the illness was a reaction to some definite physical factor—e.g., severe and prolonged pain—rather than to purely psychological events. This effect was evident no matter what type of operation was employed, although it was slightly more marked with the modified technique. It followed, therefore, that, if "endogenous depression" was simply a type of reactive depression in which there was minimal environmental cause for distress, then the results of leucotomy should be best in those cases where there was least evidence of an external cause—that is, in the truly cyclical or manic depressive cases. This had not been the experience in this series. Leucotomy appeared not to affect the enduring physical basis of cyclical depressive illnesses; the periodicity of the attacks was unaltered, although the intensity or elaboration of the depressive spell was diminished. Dr. Elithorn concluded that some endogenous depressions were prognostically and aetiologically distinct from most reactive depressions, and that leucotomy had a specific but only transient effect on the mechanisms underlying endogenous depression.

### Ten-year Follow-up of Standard Prefrontal Operation

Dr. MAURICE PARTRIDGE presented the long-term results in 96 patients upon whom Mr. Wylie McKissock had performed a standard prefrontal leucotomy some 10 to 12 years earlier and who had recently been followed up again. (They were the first 96 of the 300 reported on by the speaker in 1950†.) The incidence of epilepsy in these cases had increased in the intervening years from the 10% originally reported to 15%. Of the schizophrenics, those with affective colouring or who had had remissions prior to the operation

*Garmany, G., *Brit. med. J.*, 1958, **2**, 341.
†Partridge, M., *Pre-frontal Leucotomy: A Survey of 300 Cases Personally Followed Over 1½–3 Years*, 1950. Blackwell, Oxford.

did best and those with a progressive course before the operation least well. About one-third of these schizophrenic patients remained out of hospital, although some lived in sheltered circumstances. Cases of affective disorder did better, but continued to have recurrences, though these were milder. Seven previously incapacitated obsessionals had been able to live an approximately normal life without relapse. Seven of the 96 had died from causes unconnected with the operation; of the 89 survivors, 46 had been able to remain continuously out of hospital for 10 to 12 years.

### Rostral Leucotomy

Mr. WYLIE MCKISSOCK then described his more recent experience with rostral leucotomies. When it was recognized that the earlier types of prefrontal leucotomy often produced undesirable personality changes, modifications of technique had aimed at producing a smaller and more accurately localized lesion, he said. Since 1948 he had carried out rostral leucotomy in increasing numbers. In 1957, for instance, of 144 leucotomies he had performed 125 were rostral and only 19 a standard Freeman Watts. After Pippard's report of some personality changes of undesirable kind in the rostral (G) operation he had modified his technique, taking a more forward line of section, now directed towards the midpoint of the orbital plate. He called this operation rostral (P).

There had been a distinct change in the type of case referred for operation—fewer old schizophrenics and more cases of tension, agitation, or depression. In his series of 490 rostral leucotomies, the mortality of less than 1% emphasized the safety of the procedure. Nor did the operation require any specialized apparatus or equipment. In a series of 60 rostral leucotomies he had performed at one hospital there was a recovery rate of 60%, while a further 30% had been discharged from hospital although not working. These figures could be compared with recovery and discharge rates of 39.6% and 13.5%, respectively, in a series of 111 prefrontal leucotomies performed in the same institution. When the cases submitted to rostral leucotomy were separated into those with depressive and those with other psychotic illness it appeared that the best results were obtained with the depressives. Thus 25 of 38 depressed patients were discharged and working and a further 11 were discharged but not working. For the other psychotic states, the corresponding figures were 6 out of 17 discharged and working, and a further 7 discharged and not working. These differences were also seen in the prefrontal series. Of 5 cases of obsessive compulsive states, all were discharged and working. Rostral leucotomy had proved itself to be a form of treatment with a very low risk to life and to have remarkably few side-effects. If used in properly selected cases, it offered a high rate of recovery.

### Orbital Undercutting

Mr. GEOFFREY KNIGHT said that, influenced by the results of animal experiments and Rylander's observation that lesions in the orbital aspects of the brain would produce tranquillity and loss of fear, he had followed in a modified way since 1949 Scoville's method of orbital undercutting. He used a more limited incision so as to disturb as little as possible the more lateral fibres subserving emotional appreciation and intellectual processes. The operation, although a long one taking up to two hours, was worth while because it resulted in the absence of all undesirable side-effects such as grossly increased appetite, adiposity, and incontinence. There was no intellectual blunting, the patients felt relaxed, and remained warm individuals with normal emotional reactions. In three cases a second operation at the same site, by extending the lesion, resulted in success.

Mr. Knight then analysed the results in the first 167 cases he had followed up out of a total of 250 treated in this way. Of 53 cases classified as "psychiatrically disabled" (in the sense that although out of hospital they were in need of

*(Continued at foot of next column)*

# To-day's Drugs

*With the help of expert contributors we publish below notes on a selection of drugs in current use.*

**Marcoumar** (Roche Products Ltd.).

**Marevan** (Evans Medical Supplies Ltd.).

These are preparations of warfarin sodium, which is the sodium salt of 3-(α-acetonylbenzyl)-4-hydroxycoumarin, and is chemically closely related to dicoumarol. Like dicoumarfol, warfarin in an anticoagulant which exerts its effect by interfering with the hepatic synthesis of prothrombin.

There are now a number of anticoagulants, most of them closely related chemically, that are available for clinical use. These include the earlier preparations, dicoumarol and ethyl biscoumacetate, and the more recent one, phenindione. Warfarin exerts its full therapeutic effect earlier and more constantly than dicoumarol and ethyl biscoumacetate. Fremont and Jagendorf[1] have claimed that marevan is superior also to phenindione in this respect, producing an initial effect within 18 hours and exerting its full therapeutic effect by 36 hours. Warfarin also appears to be a stable and predictable form of maintenance therapy, and frequent alteration of the dosage has been found unnecessary.

Toxic reactions are similar to those produced by other anticoagulants, but so far complications from haemorrhage have not been serious and respond quickly to vitamin $K_1$. The indications and contraindications are the same as for other anticoagulants.

The initial dose is commonly between 35 and 50 mg., depending on the weight of the patient. Maintenance dosage depends on the results of prothrombin estimations, which are necessary for satisfactory control of the therapeutic effect and prevention of complications.

N.H.S. basic price: marcoumar, 25 3-mg. tabs., 5s.; marevan, 100 3-mg. tabs., 32s. 6d.

REFERENCE

1 Fremont, R. E., and Jagendorf, B., *J. Amer. med. Ass.*, 1957, **165**, 1381.

**Actal** (Bayer Products Ltd.).—Each tablet contains sodium polyhydroxyaluminium monocarbonate-hexitol complex in tablets of 360 mg. This is an elegant preparation of aluminium hydroxide. The tablet has a pleasant taste, dissolves readily in the mouth, and, being an antacid rather than an alkali, will not cause alkalosis. Like all preparations of aluminium hydroxide it is somewhat constipating. There is no published work on this preparation; it is therefore impossible to say whether any advantage it may possess over the ordinary *B.P.* tablet of aluminium hydroxide is sufficient to justify the disparity in price between them.

N.H.S. basic price: 48 tabs., 4s. 3d.

*(Continued from preceding column)*

constant psychiatric help) 35 fully recovered and a further 14 improved enough to carry on without psychiatric help, in spite of slight symptoms; of 44 "socially incapacitated" (out of hospital but not working) 31 fully recovered and 8 improved; and of the remaining 70 cases who were "totally disabled" (in mental hospitals) 43 fully recovered and 19 improved. In the whole group there were two deaths, both hypertensive cases, and six patients developed epilepsy. The highest recovery rate (75%) was obtained in the group with anxiety and tension states, followed by those with depression (66%), obsessional states (61%), and lastly schizophrenia (44%). The operation relieved cases of agitation and depression in which all other forms of treatment had failed and where the illness had been present for 10 years or more. This suggested that there might be a case for its earlier employment in some of these cases.

# Correspondence

*Because of heavy pressure on our space, correspondents are asked to keep their letters short.*

## Medicine on Television

SIR,—A change of role to that of patient prevented me from hearing Mrs. Mary Adams and Mr. Dickson Wright discussing "Medicine on Television" (*Journal*, November 29, p. 1351), but Professor Roger Warwick's letter (p. 1354) has brought some of the flavour of it to me. My long interest in non-medical sound broadcasting and television, sadly and unprofitably restricted by the fact that these are not the most suitable spare-time occupations even for full-time doctors, has provided me with enough experience of several of the B.B.C.'s services to realize that a revolution is taking place in adult education. The desire of what we choose to call "backward peoples" to know about the world in which they live and how it works, and to hear what others have thought about it, makes most of our programmes seem extremely frivolous. Some small countries demand continual talks of a kind which would only be tolerated here by the few and would have to be put on at the most inconvenient times.

Television is an even more astonishingly influential means to adult education which has burst upon us all unprepared. There is a particular demand for public education in medicine. It is not clear why we should call a growing desire to understand what goes on in nuclear physics as enlightenment and the same inquiry in medicine as morbid curiosity. Since we are going to have medical television programmes whether we like them or not, we do well to consider the principles which might govern their presentation. For my part I think that first and foremost they should be entertaining. I consider that the B.B.C. started well long ago at Alexandra Palace when Mrs. Mary Adams and Andrew Miller Jones had a policy. Then they presented an account of how things worked, some simple demonstrations in physics or physiology, and related this to a simple human story. In later programmes the influence of advisers has been seen, results have been presented without previous explanation, and some have even sunk to exhortation and propaganda. The old programmes were entertaining and educational, the newer (with a few fine exceptions) have too often been peeps behind the scenes with the nasty bits glossed over or inexcusably dull.

To finish on a controversial note, my pet aversion on the television screen is the anonymous doctor. To me he appears as a superior expert whose credentials I cannot check, who sets himself apart from ordinary folk by a secrecy which enhances that personal mystique which is at the heart of most of what is phony in medicine.—I am, etc.,

Knockholt, Kent. D. W. SMITHERS.

## Cause of Post-vagotomy Diarrhoea

SIR,—In an earlier paper this year Burge and Pick[1] stated that the cause of diarrhoea following vagotomy and gastro-enterostomy for chronic duodenal ulcer was not known. It was mentioned in this paper that this problem was being investigated in the Medical School of the West London Hospital. This symptom has been generally thought to arise from intestinal infection due either to reduction in gastric acid or to post-operative gastric stasis.

As a result of our work we have evidence that this symptom is caused by pancreatic insufficiency resulting from vagal denervation which must follow division of the main posterior vagal trunk. This work will be reported in detail in the near future. Meanwhile, surgeons who use this operation are urged to preserve the coeliac division of the posterior vagus while dividing all its gastric branches. This is easily done by dividing the small omentum completely from the pyloric antrum. The left gastric artery and vein are divided close to the stomach. In this region the main gastric division of the nerve is easily seen and divided, leaving the coeliac division passing posteriorly to the coeliac plexus.—We are, etc.,

HAROLD BURGE.
PETER CLARK.
LESLIE CHAPMAN.

West London Hospital Medical School, London, W.6.

REFERENCE

[1] Burge, H., and Pick, E. J., *Brit. med. J.*, 1958, 1, 613.

## The Art of Consultation

SIR,—May I send you a brief note to express my appreciation of Dr. G. F. Abercrombie's excellent James Mackenzie lecture on "The Art of Consultation" (*Journal*, November 29, p. 1349)? In a way I find myself fortunate, for I was for some years a general practitioner before taking up surgery as a specialty. I am thus able to see from both sides the problem which he presents. In my later years as a consultant I cannot tell how much I owed to the many excellent general practitioners of Northern Ireland. Especially would I like to pay tribute to the late Dr. John Taggart, who strangely enough was an assistant to Dr. James Mackenzie when he was a general practitioner in Burnley before going to London, and the latter never forgot what he owed to the years he spent in general practice.

Dr. Abercrombie draws a clear distinction between a consultation and a second opinion. This is, I think, a vital problem to-day. Surely the failure of consultants to meet G.P.s, and vice versa, is one of the tragic defects in the present N.H.S. (at least in Northern Ireland). In former times those meetings were the very bread-and-butter of consultants. To-day I understand many part-time consultants and all those on full time never want to see a general practitioner. Why is this? Do they foolishly think that the G.P. has nothing to contribute to the average consultation?—I am, etc.,

Belfast. S. I. IRWIN.

## Poliomyelitis Vaccine

SIR,—Your leading article and the articles on live poliomyelitis vaccine (*Journal*, November 15) are valuable contributions on this important but controversial subject. However, it would appear that some clarification of the technical policy of the World Health Organization in this connexion is necessary in order to avoid possible misunderstanding. All Expert Committee Reports carry on their cover the statement that "this report contains the collective views of an international group of experts and does not necessarily represent the decisions or stated policy of the World Health Organization." In this instance the policy of the Organization is in substantial agreement with the recommendations of the Committee, although it may be that there are differences in the interpretation of certain recommendations.

The statement quoted in the leading article (p. 1210) to the effect that "tests on hundreds of thousands of people will be necessary to establish whether the theoretical expectations of safety can be confirmed in actual practice" is, in its context, a statement of fact and not a recommendation that such tests be carried out now. Since it is not known what the currently used tests on monkeys mean in terms of safety for man, it is obvious that only actual tests on man on a sufficiently large scale will finally prove the innocuity of a strain. These large-scale tests should not be carried out until there is good presumptive evidence of safety and stability, based both on laboratory and on small-scale human studies. The Expert Committee insisted most strongly on the need for a cautious extension of strictly controlled human trials under the most careful supervision. The criteria which should be fulfilled were specified in some detail. So far W.H.O. has not given direct support to any trial of live poliovirus vaccine, and, contrary to some reports, the "test" in the Belgian Congo was not supported by W.H.O. The Organization has of course

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**the lines of communication"**

**in psychosomatic**

**(stress or functional)**

**disorders**

Bellergal Retard blocks the passage of excessive stimuli from psyche to soma via the autonomic nervous system.

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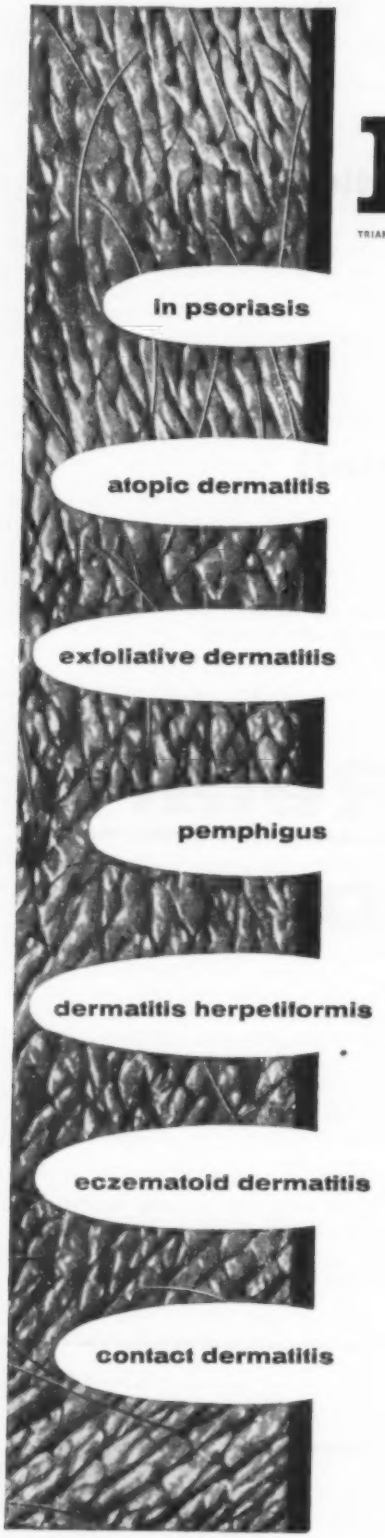


# Ledercort*

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## in the control of psoriasis and other dermatoses

Studies[1] confirm that LEDERCORT triamcinolone gives symptomatic relief on a substantially lower dosage than other steroids, and fewer side effects. It has been reported[2] that 36 of a series of 60 patients with psoriasis responded rapidly and dramatically to LEDERCORT in doses of 12 to 16 mg. daily. In some patients, the psoriasis was completely erased within 2 to 4 weeks.

[1] *J.A.M.A.* *165*: 14: 1821-1823 (Dec. 7) 1957.
[2] *J.A.M.A.* *167*: 8: 959-964 (June 21) 1958.

**Ledercort**

*Oral tablets scored for easy division. 2 mg. Bottles of 30 and 100. 4 mg. Bottles of 30, 100 and 500*

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followed closely the scientifically conducted studies which are in progress in several countries, and it is clear that a great deal of new information will become available in the coming months on which future policy may be based.

The Director-General made the present position of W.H.O. clear in a statement to the Eleventh World Health Assembly in May, 1958, in which he said that W.H.O. was not satisfied with the evidence for the stability of the available strains and did not support large-scale trials of this vaccine at the present time. He emphasized the need for caution, pointing out that the availability of a safe and effective inactivated vaccine greatly reduced the urgency of developing the live virus vaccine.

With respect to the statement by Professor G. W. A. Dick and Dr. D. S. Dane (p. 1184) that the Expert Committee virtually ignored the problem of spread of the vaccine virus, I can assure them that the problem was carefully discussed and that it was one of the important reasons behind the strong recommendation for the most careful supervision of field trials by someone experienced in investigations involving poliovirus, who would therefore be fully aware of the danger of spread. I have myself repeatedly called attention to this problem, both in publications and in communications to those proposing to use the vaccine. Some carefully designed trials to throw light on this important problem are in progress and the results may be expected in a few months.—I am, etc.,

A. M.-M. PAYNE,
Secretary to the Expert Committee on Poliomyelitis.

World Health Organization, Geneva.

## Pharmaceutical Houses and the Doctor

SIR,—It would be a great pity if Dr. Mary Rayner's letter (*Journal*, November 22, p. 1291), or any replies to it, were allowed to imperil the good relations which exist between the pharmaceutical industry and the profession.

We in the industry are aware that some members of the profession are at times critical of us, but I can assure you, Sir, that we take note of such criticisms, taking care to put it into perspective, to determine the validity, and to take whatever action is necessary. Our job is to provide the tools of clinical medicine. To do so we must bring the results of our efforts to the clinician as quickly as possible.

The alternatives to co-operation and understanding are acrimony and prejudice; as we are indispensable to one another let us pursue the first course.—I am, etc.,

T. H. M. KERFOOT,
President,
The Association of British Pharmaceutical Industry.

London, W.C.1.

SIR,—I agree entirely with Dr. Mary M. Rayner and Dr. Charles S. Thompson (*Journal*, November 22, p. 1291). Neither of them, however, mentioned a new form of advertising which appears to have crept in. I refer to the discussion in the doctors' columns of newspapers and women's magazines of drugs, mentioned by name, and in certain cases with the maker's name and cost, and the implication that the reader may well ask his doctor for these drugs.

I do not suggest that the drug houses are responsible for this. Nevertheless, I feel that drugs so mentioned have moved into the class of the publicly advertised aspirin derivatives, and I wonder whether one should continue to prescribe them, good though some of them may be. To whom are those who write these articles responsible, and is there no way of restraining them?—I am, etc.,

R. HEWITT.

Salford, 6.

SIR,—I was most interested in the letter of Dr. Mary M. Rayner (*Journal*, November 22, p. 1291) and find myself in agreement with many of her views.

I wonder how many of my colleagues recently received a sample of antacid tablets in a wedding cake presentation box. At my home it was opened with pleasurable anticipation, and we were well and truly "taken in." My first impulse was to return a similar package containing senna pods to the managing director of the firm responsible, but second thoughts prevailed. Instead I wrote to him saying that this kind of salesmanship was not appreciated and to cross us off the mailing list. I should have known better. In reply I received a long letter which, using military language, may be divided into three parts. Firstly, the retreat; with the expression of sorrow that their efforts to present their products in a humorous and rather different style, etc., had not been appreciated. Secondly, the marshalling of the forces; with an exposition of the merits of the firm. Finally, the attack; with a final paragraph turning the knife in the wound by describing in detail the efficacy of the first-mentioned antacid tablets.

"What kind of a people do they think we are?"—I am, etc.,

H. S. SPILLER.

Bearwood, Smethwick.

SIR,—Reading through the correspondence columns in the *British Medical Journal* recently, I have been struck by the attack on the pharmaceutical houses. It appears to me that much of this is unwarranted and that insufficient credit is given where credit is due. It is common knowledge that, as a result of money invested by them in research, they have given to the medical profession a number of very valuable drugs which have provided the doctor with powerful weapons in his fight against disease. Of course the pharmaceutical houses are profit-making concerns which must advertise and sell their products, but the criticism often levelled against them, that their prices are excessive, has not been substantiated. Indeed, on looking through a recent official publication giving the cost of proprietary and official equivalents,[1] I was impressed by the large number of cases in which the cost of the proprietary preparation was no greater than that of the official, and in a few cases was even less. Moreover, there were a large number of drugs which were considered to be of such value as to be included in the *British National Formulary*, but which are available only in proprietary form. These are evidently the result of original research on the part of the pharmaceutical houses.

But the chief concern of correspondents seems to be the manner in which the pharmaceutical houses keep us informed of their products and their efforts to urge us to prescribe them. This is done by advertisements in the journals, by mailed literature, and by visits from representatives. Personally, I peruse the advertisements, sort the mailed literature, discarding the more sensational and filing the more informative, and enjoy a short discussion with representatives. But surely those who are not so inclined can deal appropriately with the postal advertising; and, after all, we who are accustomed to handling all manner of patients can surely deal with representatives in, I hope, a courteous manner.

As a former practising pharmacist, I was interested to read Dr. Mary M. Rayner's comment (*Journal*, November 22, p. 1291) on extemporaneous oral penicillin preparations, and I would very much like to see her prescription for a stable, elegant, and palatable preparation of oral penicillin, comparable to the proprietary products. Finally, if we are unable critically to appraise the literature sent to us and evaluate the pharmaceutical preparations for ourselves, then we have no right to be prescribing for our patients. And if, as Dr. Rayner suggests, we are treated as a band of immoral morons, then we have only ourselves to blame.—I am, etc.,

JOHN E. PEARSON.

London, S.E.4.

REFERENCE

[1] N.H.S. Pharmaceutical Services, Costs of British National Formulary and Proprietary Preparations, July, 1958.

SIR,—Dr. Mary M. Rayner (*Journal*, November 22, p. 1291) and other correspondents are concerned about the propaganda methods of the drug houses. I would like to make a few comments.

The practice of consigning advertising matter to the waste-paper basket seems to me deplorable. We all use a proportion of proprietary drugs, and it is surely our duty

to keep up with the literature about them. I open all advertising matter once or twice a week over a large metal waste-paper basket (specially purchased). Most of it is familiar or of no interest, but perhaps 5% is important, and this I read or keep for reference. About 15 minutes per week is sufficient for this. I find it a tedious chore but worth while, and the very last thing I would wish to encourage is "a body of men" who would do this for me and no doubt before long tell me exactly what I might prescribe. Dr. Rayner gives oral penicillin as an example of a drug with a multiplicity of trade names. Maybe it has, but there is no need to specify any of them. It would still be necessary to know the varieties and dosages of oral penicillin if there were no proprietary preparations at all —in fact, to know how to write a prescription.

Dr. Rayner must cease to be sentimental about the representatives and stop giving them interviews, for otherwise she is conniving with the drug houses to give a service of which she disapproves. As I read the literature. I rarely find it necessary to trouble the representatives. When "caught" I find it best to head them off the latest "epic discovery" and get them on to motor-cars, a subject on which they are often very well informed.—I am, etc.,

Derby. G. N. L. GODBER.

SIR,—I am not one of those who despise travellers. Indeed, I seldom fail to learn something from them. After all, the man (or woman) who excluded all travellers and never opened an advertisement might miss quite important advances. The great things done in this century by the pharmaceutical firms put all humanity in their debt. At the same time, the weight of correspondence makes it almost impossible to pick out the good from the bad.

I foresee more drastic measures to gain our attention—auroscopes, proctoscopes, car-rugs, cigars, and later holidays at sea are ideas that occur to me. Employees of British Railways can go to Brindisi free. In what way are we inferior to those admittedly deserving and undoubtedly stout fellows who drive our trains? I hope enterprising firms will take the hint.—I am, etc.,

London, N.W.4. R. W. COCKSHUT.

SIR,—Dr. Mary M. Rayner is right when she states (*Journal*, November 22, p. 1291) that the standard of prescribing in general practice is low. How can it be improved? Of course better undergraduate teaching is fundamental, but to my mind so are the following: (1) The maximum size of panel lists should be reduced, because less busy surgeries mean more time for thought, diagnosis, and treatment, and more time for reading in the evenings to improve one's knowledge (and this includes reading the morning mail, some of which is highly informative). (2) Postgraduate courses should be more widely available and periodic attendance at them should be obligatory. I do not mean week-end courses at the local hospital or clinical afternoons or evenings, but comprehensive courses in big centres by recognized teachers. If the public were to become aware that all general practitioners received regular postgraduate tuition, surely this would help to raise the status of general practice.

I have talked with numerous fellow general practitioners on the subject of drug-house representatives and I find that on the whole they do not resent them. My own view (frequently shared) is that some are too young and lack good presence and diction. I have not discussed this subject with any specialists, but I have seen no letters of complaint from them, so perhaps they are satisfied. But if the profession as a whole wants any change in their personal contact with the drug houses, something had better be done about it soon, because there can seldom have been such a spate of advertisements in the national press for additional "reps" by the industry as there has been recently. I have wondered whether the industry could seek some of their recruits from those now coming out of the Services, some of whom apart from having the necessary aptitude for training must have a knowledge of Continental languages and are familiar with Continental travel and hotels, and who could take and show British-made drugs, many of which are so excellent, to our colleagues abroad. Perhaps this is the general custom now except in those countries that restrict their imports of pharmaceuticals. But free trade throughout Western European countries is still a possibility in the early future, and this may well provide a striking opportunity for our pharmaceutical industry to expand.

We have heard often enough that British industry as a whole is not forceful enough in its foreign sales promotion. In the medical press we read letters of complaint that the home sales promotion of the pharmaceutical industry is distasteful. It may be that this is a subject fertile for research.—I am, etc.,

Folkestone. G. R. FABER.

## Antihistamines in the Treatment of Burns

SIR,—In 1949, soon after I had a letter published in the *Lancet* on the use of antihistamine drugs in the treatment of burns,[1] I applied to the Home Office for an experimental licence to continue my chance observations on humans by animal experiments. I was refused a licence. Now I note that Dr. D. L. Wilhelm and Miss Brenda Mason (*Journal*, November 8, p. 1141) have got one for the same line of work—but at the Lister Institute, which is proof that their research will be "respectable." It is no use talking about encouraging general-practitioner research, and then granting experimental licences only to people with the rubber stamp of institutions whose founders or namesakes were not plagued with the need for permits to experiment.

Nevertheless I am pleased that someone else has noticed that antazoline is relatively less effective in the treatment of burns, which explains why Sevitt *et al.*[2] failed to note much effect with four volunteers given antazoline for small circular experimental burns. Although your *Journal* was good enough to publish letters by Herxheimer[3] and others soon after pointing out this lack of potency, yet the treatment of burns has been held up over six years. Now that the antihistamines are a respectable part of anaesthesia opportunities to observe their effects in burns are greater.

Even with antazoline, if one employs an effective dosage—for example, 100 mg. intravenously in an adult and repeated as needed (about twice the dosage Dr. Wilhelm and Miss Mason mention)—rapid relief of pain can be noted in burns much older than the ten-minute limit for effect which they find.

As I noticed years ago, dosage must be large enough and continued long enough to neutralize most of the histamine formed. A day-old burn will have had more irreversible damage done, and more histamine will have been released than from the same burnt area after only a few minutes; histamine release goes on for over a week. I hope Dr. Wilhelm and Miss Mason will go on to human burns.—I am, etc.,

Manchester, 16. S. SHUBSACHS.

REFERENCES

1 Shubsachs, S., *Lancet*, 1949, **1**, 936.
2 Sevitt, S., Bull, J. P., Cruickshank, C. N. D., Jackson, D. M., and Lowbury, E. J. L., *Brit. med. J.*, 1952, **2**, 57.
3 Herxheimer, H. *Ibid.*, 1952, **2**, 228.

## Buzzers for Bedwetters

SIR,—Since your original annotation on this subject (*Journal*, August 23, p. 499) the ensuing correspondence has only served to confuse me as to the issues involved. On the one hand the practically minded speak highly of the buzzer method, and their results in terms of stopping bed-wetting are excellent. On the other hand there are those who consider the buzzer method cruel and recommend more "normal" methods, including treatment of an assumed underlying mental condition and forcing the child to drink large quantities of water (Dr. D. Saklatvala, *Journal*, September 13, p. 690, and Dr. G. H. Gilford, *Journal*, October 11, p. 918). One correspondent (Dr. Gordon Ambrose, *Journal*, October 4, p. 859) seemed to regard the buzzer-treated child as an abnormal one who required hypnosis under which it was told that the buzzer means getting up and *not* passing water. If this does not cause the child confusion it certainly adds to mine.

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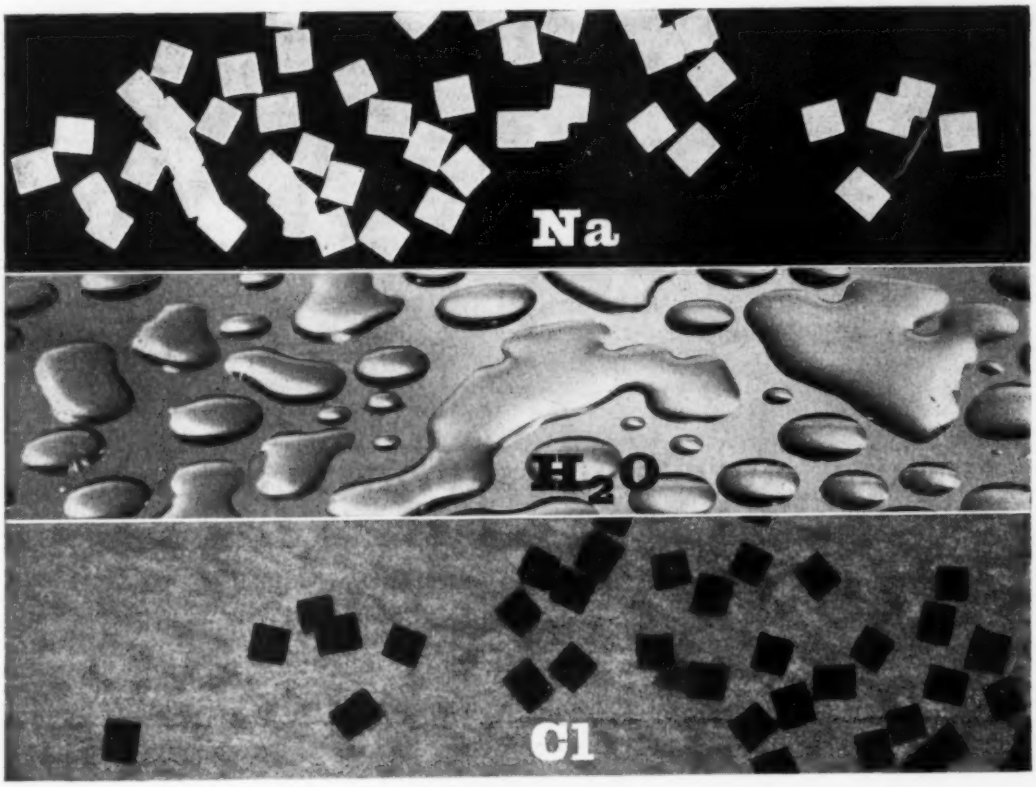


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I am therefore particularly grateful to Dr. W. Ritchie Russell (*Journal*, November 15, p. 1227) for his reassuring views on the matter. I too am surprised that anybody should think the buzzer method harmful. I am sure that all these children (and their mothers) are delighted that the enuresis has been cured within a few months, and I venture to suggest what Dr. Ritchie Russell implies, that very few will require additional or subsequent psychotherapy. It is a pity that someone cannot conduct a controlled trial of a psychiatric approach versus the buzzer method. Unfortunately, although this would show which method cured bed-wetting best, a long follow-up would be demanded by the psychiatrist to assess the development of subsequent mental disorder. I would counter this by following up their unsuccessful cases and assessing the effects both on the child and other members of the family. I again suggest that the balance would be very much in favour of the buzzer.

Finally, I feel I should point out that my own experience in the treatment of enuresis is very small, in fact the only case I can call to mind was in a boy of 9 who was under my care when I looked after the Families' Medical Centre in the Army.

When I was treating another child in the family the mother told me about the bed-wetting of the boy in question. He had been seen by a psychiatrist a month previously, who had told her that the child should be allowed to play with water as much as he liked. She complained bitterly that he was no better and in addition now made a terrible mess during the day. I did not wish to interfere and told her to persevere and be patient. I did not see her again until two months later, when I met her in the street. I inquired about the bed-wetting and she told me that there had been no trouble for over six weeks. I suggested that she must be very pleased with the advice she had received. From the way she looked at me I knew there was more to tell, and after a good deal of hesitation she confessed that one morning soon after I had last seen her she had got so mad at the sight of another wet bed that she had struck her son several times with a coat-hanger. She was very sorry for this afterwards and was glad she had got it off her chest to me. When I last saw that family they all seemed very happy and there had been no return of the bed-wetting.

To anticipate further correspondence, I would hasten to add that I am not recommending the "coat-hanger method," even though it is cheaper than the buzzer.—I am, etc.,

London, S.W.10. DENIS BURLEY.

### Post-parotidectomy Gustatory Sweating

SIR,—The correspondence on this syndrome has been both interesting and instructive, but any theory to explain the phenomena must take into account the following data: (1) The syndrome may follow total or partial parotidectomy, or even only injury to the gland. (2) It only does so in about 25% of the cases after total conservative parotidectomy. (3) It occurs whether the external carotid artery has been ligated or not. (4) It can occur after an apparently successful resection of the auriculo-temporal nerve. (5) Either flushing or sweating or both may occur in the area supplied by the auriculotemporal nerve or, more rarely, the great auricular nerve. (6) Only part of the area supplied by either of these nerves may be affected. (7) Sweating can occur with or without loss of cutaneous sensation in the area supplied by the auriculo-temporal nerve. (8) The incidence of the syndrome is considerably reduced, but not abolished, by resection of the auriculo-temporal nerve. (9) Sympathectomy does not abolish the syndrome but otic ganglionic block does.

I have personally rarely ligated or dissected the external carotid artery and have almost always removed the whole of the gland. In my last 20 cases I have tried to avulse the auriculo-temporal nerve. The reason this auriculo-temporal nerve avulsion may fail is that only the cutaneous branch may be avulsed, leaving the deeper motor secretory nerve intact.

The theory which seems to me to take into account all the data is that, when the parotid gland is traumatized or resected, the multiple fine branches into which the motor secretory branches of the auriculo-temporal nerve divide become united in some cases with the sympathetic branches surrounding the external carotid and superficial temporal arteries which have likewise been sectioned at the same time. Stimuli from the tongue then pass along the motor secretory branch of the auriculo-temporal nerve and reach that part of the skin that is supplied by the sympathetic branches with which they happen to have united. This flushing or sweating may occur over any area according to the particular branches of the sympathetic nerve which have become anastomosed; clearly this will vary with the individual's power to form such successful anastomoses. Therefore this gustatory sweating may best be prevented by resecting the external carotid artery and a large part of the superficial temporal artery together with their perivascular sheaths. At the same time, resection of the anterior portion of the auriculo-temporal nerve will prevent the sweating occurring in those rarer cases in which the main auriculo-temporal nerve has been sectioned and a cross union of the motor secretory and the cutaneous branch has later occurred.—I am, etc.,

London, W.1. HENRY A. KIDD.

SIR,—In their article on post-parotidectomy gustatory sweating Messrs. D. H. Glaister, J. R. Hearnshaw, P. F. Heffron, A. W. Peck, and D. H. Patey (*Journal*, October 18, p. 942) state that it is not possible to differentiate between the "aberrant regeneration" theory and the "transaxonal excitation" theory. W. C. Wilson[1] reported a case of post-gustatory sweating ten days after sympathectomy, on the side of operation. In view of this observation it is difficult to see how aberrant regeneration may not be the explanation of some cases of "Frey's syndrome."

However, Wilson also described a case of syringomyelia in which there was post-gustatory sweating, and this was abolished on one side by unilateral sympathectomy. Clearly transaxonal excitation or some reflex with the sympathetic nerves as the efferent arc may also be responsible for the syndrome. It is interesting that in this patient some post-gustatory sweating subsequently reappeared, and it therefore seems that in this case the abnormal sweating was produced by two separate mechanisms before and after sympathectomy.—I am, etc.,

Department of Medicine, University of Bristol. V. R. BLOOM.

REFERENCE

1 Wilson, W. C., *Clin. Sci.*, 1935, 2, 273.

### Death from Asian Influenza

SIR,—Drs. R. A. Goodbody and R. J. McGill (*Journal*, November 22, p. 1294) urge that cortisone be tried for influenzal encephalitis. In a report[1] on the neurological complications of Asian influenza we described the case history of a young girl who was unconscious and critically ill with encephalitis; her chest *x*-ray was normal. She was given cortisone and penicillin and within four hours there was marked improvement; subsequently recovery was complete.—I am, etc.,

The Cardiff Royal Infirmary, Cardiff. BRIAN MCCONKEY.

REFERENCE

1 McConkey, B., and Daws, R. A., *Lancet*, 1958, 2, 15.

### Antibiotic Therapy for Bronchitis

SIR,—I was interested to read Dr. A. H. Luscombe's letter (*Journal*, November 15, p. 1226), referring to the use of continuous antibiotic therapy for adult chronic bronchitis. Dr. Luscombe's letter exposes the unfairness of the present method of criticizing a doctor's prescribing costs without taking into consideration the possible savings which these effect by shortening the duration of the patient's illness. Dr. Luscombe is quite right when he says that the Ministry of Health is not interested in these savings, nor in the fact that a patient continues working throughout the winter. However, at a time when productivity in industry is of paramount importance, is it not time that the Ministry of Health did take these factors into account?

Dr. Luscombe asks for guidance in his problem; I would suggest he might utilize the method described by Elmes *et al.*[1] This method consists in giving bronchitic patients a supply of antibiotic tablets and an instruction to commence using these at the first sign of an onset of an exacerbation. In their paper Elmes *et al.* stated that between June, 1953, and June, 1954, male insured workers in Great Britain lost nearly 15 million days' work owing to sickness diagnosed as "bronchitis," and estimated that the cost to the community that year was about £30m. They stated that the simple measures they adopted would greatly reduce this figure, but advised that the method should be used only with patients intelligent enough to understand the instructions.

Using the latest figures available from the Ministry of Health the *total* cost of such a treatment (including chemist's profit, dispensing fee, etc.) is less than £3 10s., so that with, say, four exacerbations per year the total annual cost would be £14. The cost of keeping a patient in hospital for one week is over £23 in the provinces and £29 in London.

This factor, added to the benefits the patient and nation receive, is, I consider, a valuable argument if the Government is interested in the overall cost of bronchitis to the nation.—I am, etc.,

Folkestone. W. J. KEATING.

REFERENCE

[1] Elmes, P. C., Fletcher, C. M., and Dutton, A. A. C., *Brit. med. J.*, 1957, 2, 1272.

## Medical Education

SIR,—Having been educated in the United Kingdom, having lived in the United States, and now living and practising in Canada, I found your annotation on medical examinations (*Journal*, October 4, p. 842) most disturbing. There is a remarkable tendency these days for apparently thoughtful people in the United Kingdom to accept American methods uncritically, while at the same time they are prepared to jettison methods which have been well tried and proved in their own country for many generations. This is not to plead for the maintenance of the *status quo*. There is always room for progress, and medical education can be improved in many ways. But please think twice before accepting an American system of education, which succeeds in producing "well-adjusted morons" (an American criticism) from the schools by virtue of just some of the principles advocated in your columns: I mean "credit" advances from grade to grade, multiple choice examinations, and not permitting the poor student to fail, in case he should suffer some psychological shock. Heaven knows the Americans themselves are undergoing agonizing reappraisals of these matters since the days of Sputnik, and it is the more difficult for them as "democratic education" is deeply ingrained in the national thought, even though it leads to proceeding at the pace of the least intelligent and to a deep suspicion of all truly educated men (egg-heads).

I recall a conversation struck up with the representative of a large business organization, who had been visiting one of the largest and best-known U.S. Mid-Western Universities to interview recent graduates from the commerce faculty. These men were all wanted by industry, and had the pick of many openings at that time. "Of course," added my acquaintance, "after we get them we have to teach them to read and write." These skilled university graduates, with good technical education, had progressed through multiple-choice examinations and were virtually incapable of expressing themselves either verbally or on paper, because they had never been taught to do so. Multiple-answer examinations do have the virtue of being easy to mark. They are easy for the examiner. They do test the student's knowledge of the books. But they are not a test of a man's true calibre. Ask a man to write for three hours on one subject, and you will have a much better idea.

The credit system has defects too, and these have been discovered. For example, the percentage of passes may be seen as a reflection on the teacher's ability. You men of integrity may doubt the importance of this. We who have seen the system in action have become more cynical in this respect.

All tests of skill and knowledge are open to objections. Some able men do not do themselves justice under any system you choose to adopt. This should not obscure the broad pattern. Men of initiative and brain are on the whole stimulated by a challenge, and all of us are the more tempted to work if idleness is penalized. "When a man knows he is to be hanged in a fortnight," said Johnson, "it concentrates his mind wonderfully."

Those who decry British education may derive consolation from the fact that British speakers are renowned throughout the New World because they are so much more polished, regardless of the scientific content of their talks, and it is a fact that the standard of discussion at any medical meeting in the United Kingdom is far higher for exactly the same reason. We can certainly learn from America in many ways. Their postgraduate training is often greatly in advance of what is offered in the United Kingdom. We can learn, in fact, from their successes and their failures.—I am, etc.,

Victoria, British Columbia. KEMBLE GREENWOOD.

## Munchausen Syndrome

SIR,—I was interested in the medical memorandum on the Munchausen syndrome by Dr. J. C. Barker and Dr. T. G. Grygier (*Journal*, November 22, p. 1274).

When I was a general practitioner in London, some years ago, a lady consulted me complaining of abdominal pains, for which she requested a prescription for pethidine. She had innumerable laparotomy scars all over the abdomen; their very number, and varied sites, aroused my suspicions; also she demanded a phenomenal quantity of pethidine tablets. Discreet inquiries revealed that she was a known pethidine addict. At that time I was unfamiliar with the syndrome, although I had met the "chronic hospital patient." Unfortunately, she was more interested in seeking pethidine *ad lib.* than in obtaining treatment for her addiction, so she never consulted me again.

I was left wondering whether the addiction was the result of innumerable surgical operations, or whether the laparotomies were sought merely in order to obtain pethidine.—I am, etc.,

Hale, Cheshire. AUDREY ROBERTS.

## Charges of Indecency

SIR,—In his article on the Disciplinary Committee of the G.M.C. (*Journal*, November 22, p. 1257) Mr. C. P. Harvey, Q.C., gives an instance of how a doctor may be charged by the police with "committing acts of indecency." He appears to imply that, merely because this doctor walked home from a party through a London park at night, he was seized upon and had this charge made against him. I gather Mr. Harvey to mean that he is not suggesting that the doctor committed any indecent act in reality.

I know such things have happened—a friend of mine was charged more or less in this way and was found not guilty by the court—but is Mr. Harvey really trying to tell us that one person in every so many will be charged with indecent acts merely because he walks home through a London park at night? He does definitely make the point that the story is staged in London, and I am happy to be able to share with him the view that this would be rather unlikely to happen anywhere else.—I am, etc.,

Birmingham, 31. DAVID T. MACLAY.

## Premonition of Death

SIR,—I should like to support Dr. A. A. Lewis (*Journal*, November 8, p. 1165) in his view that we are more apt to remember those occasions when a premonition of death has proved accurate, and to forget the "false alarm." Shortly after I qualified, I was staying with my grandmother, who was then 85, and was called to her at 5 a.m. one morning as she thought she was about to die. She was thanking her two faithful maids for all their care of her, and had literally turned her face to the wall. To my inexpert eye she did not appear to be dying, and in fact she lived for another ten years, and might have completed her century if it had not been for a fracture of the neck of the femur.—I am, etc.,

Cambridge. JANET BOTTOMLEY.

⁂ This correspondence is now closed.—ED., *B.M.J.*

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*are finding that three tablets of Franol*

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astmaa ja bronkiittia sairastaville (ja heidän lääkäreilleen)

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*a good night's sleep.*

(with apologies to a completely different type of preparation)

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# Obituary

## J. A. CRAIG, M.D., F.R.C.S.

Mr. James Craig, well known as an ophthalmic surgeon, died in Belfast after a short illness in his 87th year. He was consulting ophthalmic surgeon to the Royal Victoria Hospital, Belfast.

James Andrew Craig was born on March 20, 1872, in Ballymoney, Co. Antrim, which was also the birthplace a year or two later of another eminent doctor who has recently died—namely, Sir John Megaw. Educated at Coleraine Academical Institution and at the former Queen's College, Belfast, he obtained first-class honours in the final examinations for the M.B., B.Ch., B.A.O. of the Royal University of Ireland in 1895. For the next three years he held resident appointments at the Royal Southern Hospital, Liverpool, and then went to Vienna to study eye and ear diseases. Returning to Belfast, he was appointed demonstrator of anatomy at Queen's in 1899. Two years later he was elected honorary assistant in the eye, ear, and throat department of the Royal Victoria Hospital, and in 1902 he obtained the F.R.C.S. of England. One of his first publications appeared in this *Journal* in 1906: it was on the subject of the operative treatment of detachment of the retina. Mr. Craig served the Royal Victoria Hospital faithfully until his retirement in 1937 at the age of 65. But in 1939 he returned to his old hospital post in order to release his junior colleagues for war service. He finally ceased to practise only a few years ago when he went to live in Cultra, in Co. Down.

Mr. Craig also gave unstinted service to Queen's University from the time he was appointed lecturer in ophthalmology and otology in 1913. In 1951 his distinguished work was recognized by the award of the M.D., *honoris causa*. In presenting him for this degree Professor Biggart said that Mr. Craig had been a generous benefactor to the university, and, stimulated by his gifts, Queen's would promote research in his own subject of ophthalmology. In his own specialty Mr. Craig quickly made a name for himself. He acted as one of the honorary secretaries of the Section of Ophthalmology when the B.M.A. held its Annual Meeting in Belfast in 1909, and when the B.M.A. met again in Belfast, in 1937, he was president of the same section. At one time a member of the council of the Ophthalmological Society of the United Kingdom and of the editorial committee of the *British Journal of Ophthalmology*, he was a past-president of the Irish Ophthalmological Society and of the Ulster Medical Society.

Mr. Craig was one of the early enthusiasts for skiing, and he was also a keen golfer, being a past captain of the Royal Co. Down Golf Club. His wife, formerly Miss Blanche Waldron, died in 1952, and he is survived by two sons, one of whom is on the staff of the ancient monuments inspectorate of the Ministry of Works and is also a writer and poet. Two of his nephews have been active in B.M.A. affairs—Dr. J. A. Moody, of Ilford, a member of Council, and Mr. J. C. McMaster, of Yeovil.

R. M. writes: In his early days, and for long afterwards, the specialties of ophthalmology and oto-rhino-laryngology were not divided, and James Craig quickly made himself a master of both of them. As the years passed his reputation and his practice grew in gratifying symbiosis. His diagnostic acumen was such that his opinion was accepted without question, and his skill as an operator reflected his passion for perfection. This was, in turn, easily seen in his love of beautiful things and his appreciation of "good fare, good fellowship, and good company." Of him it may be said that he became "a legend in his lifetime." His former students all over the world will long recall the clarity of his teaching, his devotion to his hospital, and his quick wit, aways lively but never wounding. He did not always suffer fools gladly, but those who sought his aid will remember his patience, his skill, and his kindness.

## Sir ALDINGTON CURPHEY, C.B.E., *M.C.*, M.D.

The Hon. Sir Aldington Curphey, president of the Legislative Council of Jamaica, and for many years a general medical practitioner in the island, died in Liverpool last month while on holiday. He was 78 years of age.

Aldington George Curphey was born in Jamaica on August 24, 1880, the son of Mr. T. J. Curphey, who came from the Isle of Man. From Wolmer's School, Jamaica, he entered Queen's University, Kingston, Ontario, as a medical student, and graduated M.D., C.M. in 1907. From then on until 1912 he held various appointments in Ontario, including those of assistant physician, assistant surgeon, and full surgeon at St. Joseph's Hospital, Hamilton, and coroner for Wentworth County. During this period he obtained, in 1909, the Scottish triple qualification. In 1912 he returned to Jamaica and became government medical officer and medical officer of health at St. Ann. From 1915 to 1919, during the first world war, he served with the 2nd British West Indies regiment as captain in the R.A.M.C. in Egypt, Palestine, and Syria. He was awarded the Military Cross in 1919 for distinguished services in connexion with the military operations in Egypt, and was also mentioned in dispatches. After the war he returned to St. Ann and settled in private practice. From 1936 to 1944 he was a member of the St. Ann parish council, eventually becoming its chairman. Nominated a member of the Legislative Council in 1945, he was appointed president of the council in 1952. For his services as major in the Jamaica Medical Corps he was appointed M.B.E. (Military Division) in 1944, and in 1952 C.B.E. (Civil Division) for public services in Jamaica. He was created a knight in this year's Birthday Honours. A member of the British Medical Association for 37 years, he was president of the Jamaica Branch in 1937–8. He became Scout Commissioner for Jamaica in 1939, and was welfare officer to the Caribbean Forces and chairman of the Jamaica Legion. During the second world war he served as surgeon-major to the Jamaica local forces, and later was honorary colonel of the Jamaica regiment. His death has deprived Jamaica of a kindly and experienced doctor and of a public-spirited citizen.

## P. N. B. ODGERS, D.M., M.Ch., F.R.C.S.

Mr. P. N. Blake Odgers, consultant surgeon to the Northampton General Hospital and formerly reader in human anatomy in the University of Oxford, died in London on November 30. He was 81 years of age.

Paul Norman Blake Odgers was born on July 3, 1877, and was brought up in Oxford. He took first-class honours in the school of natural science at Oxford and went on to Guy's Hospital with a senior scholarship in science. Qualifying in 1902, he took the F.R.C.S. in the following year, graduated B.M., B.Ch., and proceeded to the M.Ch. in 1904. At Guy's he was a demonstrator of anatomy, and he held numerous house appointments and then went down to Plymouth to be senior house-surgeon at the South Devon and East Cornwall Hospital. Interested in children's diseases, he held clinical assistantships at the Evelina Hospital and at Great Ormond Street. In 1913 he served as vice-president of the Section of Diseases of Children, including Orthopaedics, at the Annual Meeting of the

B.M.A. in Brighton. A few years before this he had been elected to the staff of the Northampton General Hospital as an assistant surgeon, and he remained in that town until 1925, when he gave up clinical practice for an academic career in Oxford. During the first world war he had served in the R.A.M.C. as a temporary major. Among his clinical papers he contributed two to this *Journal*, one on retropharyngeal fibroma (1906) and another on a case of vegetable gastrolith (1912).

Mr. Blake Odgers retired from his readership in the department of human anatomy at Oxford in 1945 and came to live in London. He leaves a widow, two sons, and a daughter.

Professor W. E. LE GROS CLARK, F.R.S., writes: Blake Odgers will best be remembered by past students and others for his long period of devoted service to the department of human anatomy at Oxford. He was appointed a senior demonstrator in 1925, and in 1931 he was promoted to the readership in human anatomy. This latter post he occupied till his retirement in 1945. As a teacher, Odgers was particularly effective because his previous surgical experience gave him the appropriate orientation for the instruction of medical students. But his success in teaching was perhaps even more the result of the scrupulous care and patience with which he dealt with the individual problems of his pupils, and the conscientious manner in which he sought to cover the whole field of topographical anatomy in his lectures and demonstrations. His earlier research work was concerned with problems of anatomical topography and applied anatomy—for example, his careful analysis of certain markings on the neck of the femur (1931), his study of the lumbo-sacral joints (1933), and his report on a case of non-rotation of the gut (1933). But his interest became more and more focused on embryological problems, and no doubt his best work was represented by his patient studies (by means of reconstruction models) of the development of the venous valves of the human heart (1935), of the pars membranacea septi (1938), and of the atrio-ventricular valves (1939), as well as by his systematic descriptions of an early human ovum *in situ* (1937) and of a presomite human embryo (1941). In 1944 he published a small *Class Book of Embryology*, which has proved of great use for routine practical classes. But, apart from his academic career, Odgers will be remembered for the kindliness and the delightful courtesy with which he maintained such affectionate relations with his colleagues and his students. The department of human anatomy at Oxford owes a great debt of gratitude for his contributions to organization, teaching, and research over a period of 20 years.

## H. I. MARRINER, F.R.C.S.Ed., D.L.O.

Mr. H. I. Marriner, surgeon to the ear, nose, and throat department of the Royal Victoria and West Hants Hospital, Bournemouth, and formerly chief assistant in the ear department at St. Thomas's Hospital, died suddenly at his home in Bournemouth on November 26. He was 66.

Humphrey Ingilby Marriner was born on August 12, 1892, the son of a Bournemouth doctor who specialized in ear, nose, and throat work. Educated at Cheltenham College and St. Thomas's Hospital, he qualified in 1919. After holding the posts of casualty officer and house-surgeon at St. Thomas's he worked for two years as house-surgeon in the E.N.T. department there, taking the F.R.C.S. of Edinburgh in 1922 and the D.L.O. two years later. He followed his father into ear, nose, and throat practice in Bournemouth, but he by no means severed his connexion with his teaching hospital, for, having been appointed chief assistant in the ear department in 1924, he came regularly to London to work in the out-patient department at St. Thomas's for a good many years. He was also at one time throat and nose surgeon to the North-eastern Fever Hospital in London. He joined the staff of the Royal Victoria and West Hants Hospital in 1923, and in later years he was ear, nose, and throat surgeon at Blandford Cottage Hospital and laryngologist to the Royal National Sanatorium at Bournemouth.

Humphrey Marriner was one of those quiet and reserved doctors who nevertheless cannot help making the pleasantest of impressions on patients and colleagues. The reverse of pushing, he had a large private and hospital practice which kept him busy for many years. Those who got to know him well, including his theatre staff, regarded him with the greatest of affection. So far as public life went he kept in the background, though he once served as honorary secretary of the Section of Oto-rhino-laryngology at an Annual Meeting of the B.M.A. But his work for young people was outstanding, for he had a deep sympathy for children who had to face life without the advantage of a normal home background. An Officer of the Order of St. John, he was county cadet officer of the St. John Ambulance Brigade.

C. E. G.-S. writes: As a surgeon Humphrey Marriner was conscientious, careful, and rather conservative. He never followed the various surgical fashions which appeared and disappeared so constantly during the 40 years he was in practice. On the contrary, he followed throughout his professional life certain surgical principles which he had learnt in his parent hospital and which, from his experience, he considered sound. So long as his results were satisfactory he saw no reason to change his ways.

As a man he was the kindest person imaginable, retiring to a fault, and devoid of all personal ambition. He had, however, strong views and strong convictions which he preferred to keep to himself or share only with his intimate friends. It is certain that he never realized how great was his influence both on his professional colleagues and on all those with whom he came into close contact. His sound common sense and obvious integrity commanded universal respect and affection.

He had a profound understanding of the needs of young people and was able to put this to practical use in his work for the cadets of the St. John Ambulance Brigade and even more so in his magnificent work in connexion with the Talbot Homes for Boys. Throughout the years he was in the habit of taking a succession of boys from this institution into his home and giving them guidance and training to fit them for taking a useful place in the community. There are many men to-day both at home and in the Commonwealth who owe a great debt to Humphrey Marriner.

After the death of his beloved sister and his retirement from the active staff of the hospital, he must have felt rather lonely, but he found company and pleasure in his church community and among his friends at the E.N.T. and Eye Hospitals, where he was always assured of a welcome.

Marriner was a bachelor and the last of his line.

## DOROTHY M. JAMES, M.D., D.P.H., T.D.D.

Dr. Dorothy M. James, an assistant county medical officer of health in Lancashire, died at Liverpool on October 15, aged 54.

Dorothy Mary James was born on July 1, 1904, the elder daughter of the late Mr. Arthur James and Mrs. James, of Penarth, Glamorgan. A distinguished student at the Welsh National School of Medicine, she graduated M.B., B.Ch. from the University of Wales in 1928, gaining a gold medal in both medicine and surgery. After holding house appointments at the Cardiff Royal Infirmary, Booth Hall Children's Hospital, Manchester, and Alder Hey Children's Hospital, Liverpool, she returned to Cardiff to take up a Cecil Prosser research scholarship in the tuberculosis department of the medical school, where she carried out some valuable original work on tuberculin. She took the D.P.H. in 1932, the Tuberculous Diseases Diploma in 1935, and proceeded M.D. in 1937.

Dr. ENID M. ROGERS writes: Most of us who were Dorothy James's contemporaries at the Cardiff medical school or were her colleagues in her later professional life are sad at her passing. She set up in practice in her home

# "IMPROVED THERAPY FOR PEPTIC ULCER"

**Extract from the American Journal of Gastroenterology, (1957) 28, 439.**

"The medication investigated is known as Roter tablets . . . The dosage employed in the treatment of gastric or duodenal ulcer was 2 tablets, taken three times a day with tepid water immediately after meals . . . this therapy is applicable to ambulatory patients."

## SUMMARY

"In a series of 155 cases of peptic ulcer treated with . . . (Roter) tablets for three to six weeks, there was immediate relief of pain in 92 per cent of cases and roentgenological healing of the ulcer in 81 per cent. The average weight gain was 7.9 lbs. and occult blood disappeared from the stools in all of the six cases in which it was found.

"The benefit provided by the medication is attributed to the minute particulation of the bismuth subnitrate, produced by a special process of trituration in association with a synergistic antacid combination.

"The special features of this medication are immediate and prolonged relief of pain, correction of gastric hyperacidity, absence of side reactions, effectiveness for ambulatory patients, and early healing of the ulcer in most cases.

"There was no acid rebound in therapeutic dosage and no adverse effects were reported."

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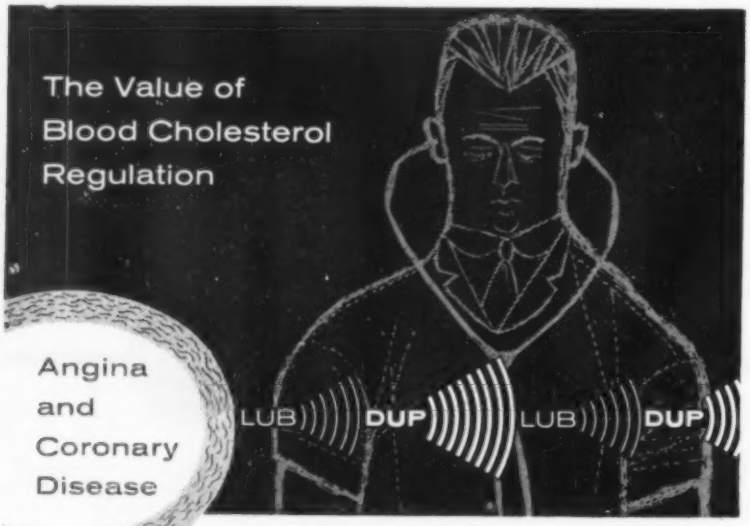


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town of Penarth for a period of three years until 1942, and was a very much loved, conscientious, and competent general practitioner. In spite of her great happiness in general practice, circumstances forced her in 1942 to make a career for herself in public health, and she became an assistant medical officer to the Lancashire health authority, with which she served until the time of her death. No account of Dorothy James's life would be adequate without a note on her personal qualities. Her integrity and quiet sense of humour were outstanding. She was a practising Roman Catholic, and in her fatal illness the spiritual strength derived from her religion stood her in good stead. To her mother and sister, all who knew Dorothy will wish to extend their sympathy.

## W. V. CRUDEN, M.B., B.S.

Dr. W. V. Cruden, who was in general practice at Brighton, died at his home at Hove on October 31 after a long illness. He was 55 years of age.

William Victor Cruden was born at Muswell Hill, London, on February 5, 1903. From Tollington School he went on to St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1927, later graduating M.B., B.S. at London University. After holding several resident appointments, including that of house-physician to the late Lord Horder at St. Bartholomew's Hospital, he eventually settled in a partnership at Brighton, where he became a much respected family doctor. During the second world war he served in the R.A.M.C. in the Middle East and Italy, attaining the rank of lieutenant-colonel. In 1956 his health became seriously affected and in the following year he had to give up general practice. During his long illness he displayed an extraordinary fortitude and found it possible to contribute to *St. Bartholomew's Hospital Journal* articles on cough, smell, and even on the subjective effects of a treatment he was receiving. He was a loyal colleague whose quiet manner and clinical acumen gave to his patients that confidence and friendliness which endeared him to them. To his widow and to his brother, also a doctor, we offer our sincere sympathy. —J. V. B.

## J. A. GUNN, C.B.E., M.D., D.Sc., F.R.C.P.

The obituary of Professor J. A. Gunn was printed in the *Journal* of November 1 (p. 1107).

Dr. R. E. M. COKE HARVEY writes: I think Professor J. A. Gunn's own account of how his *Introduction to Pharmacology and Therapeutics* came to be written may be of interest. Some 20 years ago Professor Gunn told me (his own words are reproduced as closely as my memory allows): "I was in Edinburgh turning over books in a second-hand bookshop when I came upon a bound copy of a student's notes on my lectures on pharmacology, priced 10s. 6d. Being a Scotsman, it at once struck me that if a student's notes were worth half-a-guinea, how much more profitable should a book prove to the author himself." I remember he laughed happily as he told me the story.

## T. N. WILTHEW, L.R.C.P.&S.Ed.

Dr. T. N. Wilthew, who was in general practice in the county of Durham for many years, died suddenly on November 10 at the age of 83.

Thomas Nicholson Wilthew was born at Hexham, Northumberland, on July 31, 1875. He took the Scottish triple qualification in 1912, and then set up in general practice at Sunniside, Co. Durham. During the first world war he served first in the R.A.M.C., and then went out to the Middle East as a medical officer in the R.A.F. In 1921 he returned home to build up another practice at Dunston, near Gateshead. He was proud of the fact that he started both his practices by "putting up his plate," and his patients always came first with him. He ceased to practise in 1942, but found complete retirement too quiet, so became medical referee to several insurance companies—work which he continued until 1955. A member of the British Medical Association for 40 years, he was chairman of the Gateshead Division in 1930–1. In his younger days Dr. Wilthew was a keen games player and athlete, with a particular interest in running. Later he developed a fondness for tennis, playing the game until he was almost 60 years of age. He had the misfortune to lose his wife in 1914, and is survived by his son, who is in medical practice at Low Fell, Gateshead.

## R. F. EMINSON, D.S.O., M.B., B.S., L.M.S.S.A.

Dr. R. F. Eminson, who practised in Scunthorpe, died at his home there on November 19, aged 69.

Ralph Franklin Eminson was born at Scotter in Lincolnshire on May 10, 1889, the son of Dr. T. B. F. Eminson. Educated at the Leys School, Cambridge, and Epsom College, he went on to study medicine at Charing Cross Hospital, graduating M.B., B.S. in 1911 and winning the gold medal in surgery. After holding resident posts at his teaching hospital, he joined his father in the large country practice in which he was brought up. Later he practised with his son in the steel town of Scunthorpe.

J. R. B. writes: With the death of Dr. Ralph Franklin Eminson the people of this corner of North Lincolnshire lose a good doctor and a very fine man. It must be rare to find in one locality grandfather, father, three brothers, then one son and two nephews, all of whom have been or now are medical men. Dr. Ralph was of the line of Eminson, well known round these parts for their high tradition of sound doctoring. The gentle, kind, thoughtful practitioner did not in his later years readily suggest the rugger enthusiast of hospital days, the R.A.M.C. officer whose D.S.O. and mentions in dispatches in the first world war were awarded for devotion to duty and rescue work in Flanders. His somewhat hesitant speech tended to obscure, to those who knew him little, the real value of his contributions to committee work and of his questions and comments at scientific meetings. He was a member of the local panel committee, the local medical committee, and the executive council for the County of Lindsey. A staunch supporter of the B.M.A., he was a wise and helpful member of the Scunthorpe Division and was its chairman in 1937–8. He played his part too in other local affairs and in his church, and the esteem in which he was held was shown by the mourners from all walks of life. His fortitude and calm acceptance of his long illness, which he knew must bring his life to a too early close, was an example to all associated with him. His fellow practitioners showed by their numbers at the funeral service the respect and affection they had for the doyen of the local medical profession. His wife, who died while still in early middle age, was a dearly loved and respected member of the local community, playing her part on the bench and in her church and other social spheres. To their two daughters and son, and indeed to all his close relations and to his patients, to whom Dr. Ralph Eminson was such a friend, we offer our sympathy.

## FRANK KING, M.B., Ch.B.

Dr. Frank King, general practitioner, author, and playwright, died at the Royal Halifax Infirmary on December 3 at the age of 66.

Frank King was born at Causeway Foot, near Halifax, on February 12, 1892, and was educated at Rishworth and Bradford. A medical student at Leeds University, he graduated M.B., Ch.B. in 1914, and then practised in Leeds for a time, in partnership with Dr. J. J. Anning, before entering the R.A.M.C. for service in the first world war. Soon after his return to civilian life he settled in practice at Halifax, where he remained for the rest of his life. He gave up medical practice in 1936 and thenceforward devoted his whole time to writing. Before retiring he had already written a number of successful crime stories and thrillers. His favourite creation, "The Dormouse," came later, and appeared in several of his books, the latest of which was published only last month, while another is due out early

next year. Alone, and with the Rev. L. J. Hines, Dr. King also wrote a number of plays for stage and radio, and he was closely associated with the Halifax Thespians. When the Crime Writers' Association was formed in 1953 he became a member. The authorship of over thirty books gave him great satisfaction, for he regarded writing as a recreation. He leaves a widow.

### H. M. WILSON, O.B.E., M.B., B.Chir., F.R.A.C.S.

Mr. ALAN SMALL writes: When I read Dr. Harry Wilson's obituary in the *Journal* of November 29 (p. 1360) I felt quite sad to think that the miniature of such a grand life should be so chronologically accurate and yet so unrevealing. For Harry Wilson was an interesting man both in himself and as an outstanding example of a disappearing Colonial type—a man of very great capacity, integrity, and a gift for leadership who chose quite deliberately to exert his influence and live his life in a small community in which he had his roots and for which he retained his love. His natural capacity was broadened by his training at Cambridge and St. Mary's (of whose XV he was an inspiring captain). His service to his community was fortified by the balance and integrity of his character, and by his very great skill as a doctor/surgeon. In these days of specialization we are apt to forget and even belittle the services rendered by those superior men who had added exceptional technical skill and knowledge to a basic desire to serve among people they knew. Harry Wilson was such a man. He made few mistakes and none from lack of thoroughness and care. New methods and new learning will help his successors to better his results, but there will be few to make better use of the knowledge which it is their privilege to use.

### Sir JOHN MEGAW, K.C.I.E., D.Sc., M.B., B.Ch.

The obituary of Sir John Megaw was printed in the *Journal* of November 8 (p. 1166).

Major-General HUGH STOTT, I.M.S. (ret.), writes: The death of our old friend, Sir John Megaw, leaves a lasting memory of a great gentleman of distinguished and youthful appearance and a kindly gentleness combined with a penetrating scientific mind which was so essentially practical. I first met Megaw close on half a century ago, shortly after he, Leonard Rogers, and others in Calcutta had become engrossed in the relationship between epidemic dropsy and beriberi. The Mohammedan recruits of the regiment in Southern India to which I was attached became heavily affected with symptoms indistinguishable from epidemic dropsy, which in some cases cleared leaving a residue of dry paretic beriberi. The Hindu recruits remained entirely healthy. The complete records were sent to Captain Megaw, who, with characteristic enthusiasm, asked me to stay with him, arranging for unforgettable discussions with the Calcutta Medical College physicians and with Major (as he then was) Leonard Rogers, professor of pathology. This, in 1911, was the beginning of a long friendship.

The then recently established King George V Medical College at Lucknow was indeed fortunate in having Megaw posted as its professor of pathology and principal and one of its three clinical physicians in succession to Colonel Selby, D.S.O., I.M.S. During the long war years, with his calm manner, winning smile, and devoted efficiency, Megaw built up that fine spirit which became a characteristic of the Indian staff and students of the college, and so prepared the way for the handing over of its control from the local government to that of the Indian administration of the Lucknow University. This was the first experiment of such a medical transfer in All-India. After the first world war it became my lot to succeed Megaw at the Lucknow Medical College. Manifold evidence of the fruition of his work during six years there existed on every hand, and of the extension of that harmony which already existed in the college to his colleagues in the other faculties and to the Indian administrative officials of the University. His bungalow and garden were bequeathed to me, together with his love of plants and flowers, which were, perhaps, mainly the offspring of the labours of his charming wife, who was so happy a support to him in all his social and professional work. At this time Megaw continually stressed the advantages of modern air-conditioning, then almost unknown in India, for better work-output in hot climates. Nor was he satisfied until I had personally adopted it and realized the advance it was. At frequent intervals Megaw returned as external examiner in pathology to the medical college for which he had done so much. At those visits the post-war progress of the college in all its diverse ways and the welfare of its students were always a first concern to him.

Apart from his wide clinical, scientific, and administrative abilities, it is surely for his generous humanitarianism that Megaw will be remembered. And it is certain that in present-day India his numerous old students and friends will read his obituary with affectionate remembrances and with appreciation of one of the very greatest of those officers of the Indian Medical Service who served the land of their adoption so faithfully and so well.

### F. F. STROTHER SMITH, M.D.

Colonel F. F. Strother Smith, who served in the Indian Medical Service for most of his professional life, died at Bromley, Kent, on June 21. He was 74 years of age.

Fleet Floyd Strother Smith was born on July 30, 1883. From Campbell College, Belfast, he entered Edinburgh University as a medical student, and graduated M.B., Ch.B. in 1907. He proceeded to the M.D. in 1912. Passing into the Indian Medical Service in 1908, he served at Gallipoli and in Salonika in the first world war, and was decorated with the Order of St. Sava by the Serbians. Between the two world wars he served in India in many capacities, and was appointed Honorary Surgeon to the King and also to the Viceroy. He retired from the I.M.S. in 1940, but was re-employed, and served in the second world war as a surgical and as an ophthalmic specialist in several military hospitals. Colonel Strother Smith was a nephew of the famous "Jullundur" Smith, and, using his uncle's technique for the intracapsular extraction of cataract, performed during his service very many operations, probably hundreds. He was a great lover and judge of dogs, and was at one time president of the Bull Terrier Club of India, and, latterly, chairman of the Indian Kennel Club, and a constant attendant at gun-dog trials. To his widow and family we extend our sympathy.—A. R.-G.

## Medico-Legal

### INDECENT ASSAULT UNDER PRETENCE OF MEDICAL EXAMINATION

[FROM OUR LEGAL CORRESPONDENT]

A curious but classic expedient of those whose foible is indecent assault on women is the pretence of being a medical man conducting a clinical examination requiring removal of the clothing. An example of this was recently before the courts.

A man, aged 52, pleaded guilty at Blackburn Quarter Sessions recently to two charges of indecent assault on girls, and asked for a third similar offence to be taken into consideration. His technique was to advertise in a newspaper for a magician's assistant. When a girl went for interview in answer to the advertisement he would explain that as the job entailed going abroad a physical check-up would be necessary, and he said that he was a medical man as well as a magician and was prepared to do the examination. When the girl, believing an examination to be necessary to get the job, agreed to be examined by him, he improperly assaulted her in the course of the examination.

The man, who was married to a good wife and had a family and a well-kept home, was sentenced to nine months' imprisonment.

# Medical Notes in Parliament

### Booster Doses of Polio Vaccine

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked for what proportion of children under 15 years of age, who had had two injections of poliomyelitis vaccine, the parents had agreed to a third some months later; what proportion of children had already had a third injection; and what steps were being taken to urge parents to agree to this boosting dose. Mr. WALKER-SMITH replied on December 1 that third injections started only this autumn, and by the end of October nearly 250,000 had been carried out. This represented about a tenth of the children who had had their second injection seven months or more before that date. He had so far had no evidence of parents refusing to allow their children to have third injections when their turn came. Appropriate references to the value of the boosting dose would, however, continue to be made in the publicity about the vaccination scheme.

### Medical Care Abroad

Miss ALICE BACON (Leeds, South-east, Lab.) asked with which countries the Ministry of Health had reciprocal arrangements for hospital treatment. Mr. WALKER-SMITH stated on December 1 that the Government had reciprocal social security agreements containing health service provisions which were open to all British residents in Sweden, Norway, and Yugoslavia, including tourists, and to limited classes of British nationals in Belgium, France, Luxembourg, and the Netherlands. In all cases hospital treatment was available for the persons covered. He added that discussions were in progress for a social security agreement with Federal Germany, but it was unlikely to provide medical benefit for British nationals other than pensioners resident there, and British workers.

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*Milk Consumption.*—Consumption of liquid milk in the United Kingdom in the first ten months of this year amounted to 1,264 million gallons—about 12¼ million gallons more than in the corresponding period in 1957.

*Marriage Guidance.*—The Home Secretary attaches great importance to the work of the National Marriage Guidance Council and the other organizations engaged in marriage guidance, and intends to propose to Parliament in due course that the grants shall be increased by 50% in the financial year 1959–60.

*Chiropodists.*—The registration of chiropodists is provided for in the draft scheme for the statutory registration of professions supplementary to medicine, which is under consideration.

*Hearing-aids.*—If there are no unexpected production difficulties, it is hoped to begin issues to adults towards the end of 1959 of transistor hearing-aids.

# Universities and Colleges

### UNIVERSITY OF EDINBURGH

At a meeting of the University Court on October 20 the title of honorary senior lecturer in the department of radiodiagnosis was conferred on Dr. Eric Samuel, and that of honorary assistant in the department of medicine on Dr. Jerome Rotstein, of the New York College of Medicine. Dr. Katherine M. Levy was appointed assistant in the department of public health and social medicine. The resignations of Mr. H. A. F. Dudley (lecturer in clinical surgery) and Dr. J. W. Galloway (lecturer in dentistry) were received.

### UNIVERSITY OF LONDON

The following degrees were awarded during September:

M.D.—L. S. Sacker, E. Parry-Jones.
M.S.—M. A. Birnstingh.

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN CLINICAL PATHOLOGY.—Fatima S. Ahmed, M. Y. Ali, E. F. Bowers, R. Carroll, Betty M. Clark, C. H. Coetzee, D. M. Gomez, J. W. Hill, D. O'B. Hourihane, E. B. La'Brooy, Ma Than Myint, N. Parameshwaran, L. Sefton, J. M. Uku, H. I. Williams.
DIPLOMA IN CLINICAL PATHOLOGY.—M. S. Israel, T. K. Narayanan.

# Vital Statistics

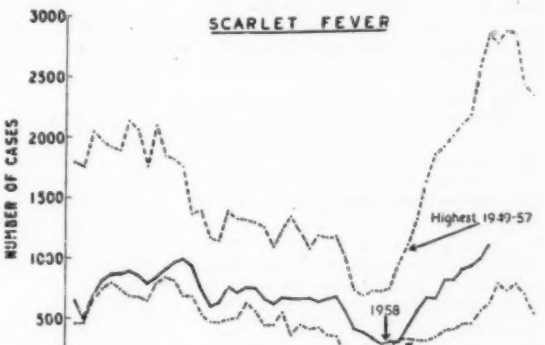
### Industrial Accidents and Diseases

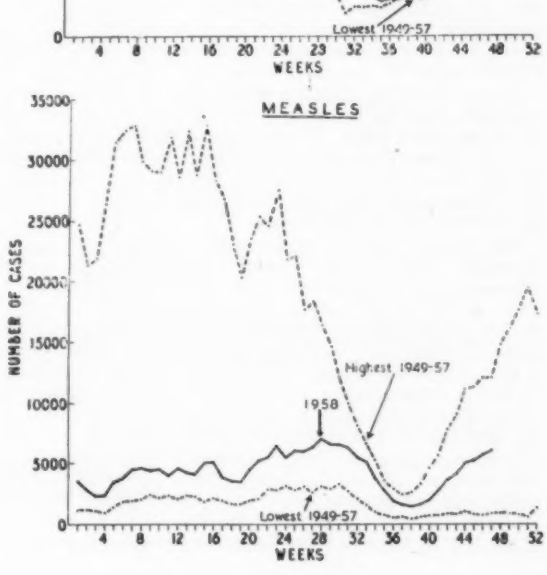
The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in October was 73, compared with 102 in the previous month and 107 in October, 1957.

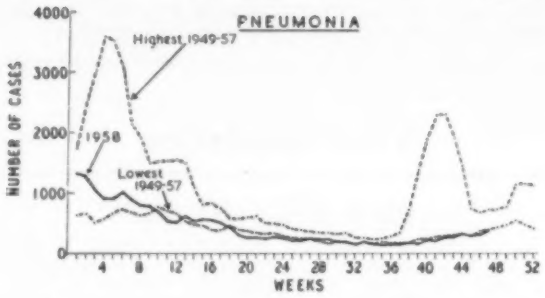
The numbers of cases of industrial diseases in the United Kingdom reported during October, 1958, were as follows: lead poisoning 10, phosphorus poisoning 2, epitheliomatous ulceration 16, chrome ulceration 14; total 42. There were 2 deaths from epitheliomatous ulceration due to mineral oil.—*Ministry of Labour Gazette*, November, 1958.

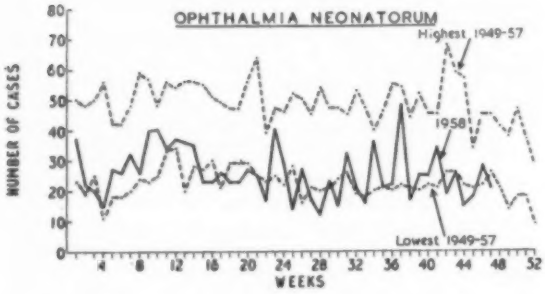
### Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus - - - - - -, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.






**Week Ending November 29**

The largest fluctuations in the number of notifications of infectious diseases in England and Wales during the week ending November 29 were increases of 798 for measles, from 6,112 to 6,910, 351 for dysentery, from 747 to 1,098, 76 for scarlet fever, from 1,088 to 1,164, 38 for acute pneumonia, from 369 to 407, and the only decrease of any size was 33 for whooping-cough, from 757 to 724.

The largest rises in the notifications of measles were 189 in Middlesex, from 250 to 439 (Brentford and Chiswick U.D. 65); 154 in Cheshire, from 349 to 503 (Stockport C.B. 87); 68 in Lincolnshire, from 246 to 314 (Scunthorpe M.B. 158); 65 in Glamorganshire, from 77 to 142 (Cardiff C.B. 100); 62 in Hertfordshire, from 79 to 141 (Elstree R.D. 85); 52 in Derbyshire, from 111 to 163 (Shardlow R.D. 66); and the only large exception to an increasing incidence was a fall of 65 in Essex, from 252 to 187. The largest fall in the number of notifications of whooping-cough was 23 in Staffordshire, from 32 to 9. No large changes were recorded in the local returns for scarlet fever. 7 cases of diphtheria were notified, being 2 fewer than in the preceding week. 3 of these cases were notified in Birmingham C.B., and a further 2 cases occurred in the outbreak in Finsbury, London.

The notifications of acute poliomyelitis numbered 69—3 more for paralytic and 6 fewer for non-paralytic cases than in the preceding week. The largest returns were Lancashire 14 (Manchester C.B. 6, Liverpool C.B. 3, Chadderton U.D. 2); Yorkshire West Riding 13 (Leeds C.B. 10); Hampshire 11 (Southampton C.B. 10); Derbyshire 5 (Shardlow R.D. 3); Durham 5 (Darlington C.B. 2).

The largest rises in the number of notifications of dysentery were 78 in Yorkshire West Riding, 76 in Glamorganshire, and 43 in Essex. The largest centres of infection during the week were Yorkshire West Riding 176 (Leeds C.B. 90, Thorne R.D. 28), Lancashire 130 (Liverpool C.B. 38, Eccles M.B. 25, Fleetwood M.B. 25, Manchester C.B. 11), Glamorganshire 124 (Cardiff C.B. 93, Rhondda M.B. 16), Warwickshire 116 (Coventry C.B. 88, Bedworth U.D. 15, Birmingham C.B. 10); London 95 (Wandsworth 22, Battersea 17, Lambeth 15), Essex 75 (East Ham C.B. 42, Epping and Ongar R.D. 16), Middlesex 51 (Hendon M.B. 33), Kent 43 (Royal Tunbridge Wells M.B. 33), Northumberland (Ashington U.D. 17), Nottinghamshire 31, Bedfordshire 26 (Ampthill R.D. 25); Cumberland 22 (Carlisle C.B. 15), and Lincolnshire 20 (Grimsby C.B. 12).

## INFECTIOUS DISEASES AND VITAL STATISTICS

### Summary for British Isles for week ending November 22 (No. 47) and corresponding week 1957

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

| CASES | 1958 | | | | | 1957 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire |
| Diphtheria .. | 9 | 5 | 9† | 1 | 2 | 4 | 1 | 1 | 0 | 1 |
| Dysentery .. | 747 | 77 | 171 | 7 | 6 | 433 | 60 | 112 | 10 | 1 |
| Encephalitis, acute | 4 | 0 | | 0 | | 5 | 2 | | 0 | |
| Enteric fever: | | | | | | | | | | |
| Typhoid .. | 3 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 1 |
| Paratyphoid .. | 9 | 0 | 1(B) | 0 | | 4 | 0 | 1(B) | 0 | |
| Food-poisoning .. | 247 | 33 | 17 | 1 | | 243 | 18 | 12 | 0 | |
| Infective enteritis or diarrhoea under 2 years .. .. | | | | 7 | 45 | | | | 20 | 20 |
| Measles* .. .. | 6,112 | 387 | 129 | 30 | 420 | 1,960 | 31 | 22 | 113 | 11 |
| Meningococcal infection .. .. | 18 | 1 | 11 | 0 | 1 | 19 | 3 | 6 | 2 | 1 |
| Ophthalmia neonatorum .. .. | 21 | 0 | 3 | 0 | | 26 | 2 | 3 | 0 | |
| Pneumonia† .. | 369 | 18 | 202 | 6 | | 499 | 28 | 280 | 7 | 61 |
| Poliomyelitis, acute: | | | | | | | | | | |
| Paralytic .. | 47 | 2 | 11 | 1 | 8 | 44 | 0 | 5 | 7 | 3 |
| Non-paralytic .. | 25 | 3 | | | | 23 | 1 | | | |
| Puerperal fever. § .. | 189 | 32 | 10 | 2 | | 217 | 33 | 7 | 0 | |
| Scarlet fever .. | 1,088 | 75 | 120 | 24 | 36 | 610 | 44 | 51 | 19 | 20 |
| Tuberculosis: | | | | | | | | | | |
| Respiratory .. | 457 | 49 | 96 | 23 | | 580 | 59 | 95 | 8 | |
| Non-respiratory | 68 | 6 | 16 | 4 | | 63 | 6 | 9 | 2 | |
| Whooping-cough | 757 | 32 | 71 | 83 | 76 | 615 | 28 | 26 | 1 | 10 |

| DEATHS | 1958 | | | | | 1957 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire | Eng. & Wales | Lond. | Scot. | N. Ire. | Eire |
| Diphtheria .. | 1 | 1 | 0 | 0 | 0 | No comparable figures available. | 0 | 0 | 0 | 0 |
| Dysentery .. | 0 | 0 | | 0 | | | 0 | | 0 | |
| Encephalitis, acute | | 0 | | | 0 | | 0 | | | 0 |
| Enteric fever .. | 0 | 0 | 0 | 0 | | | 0 | 0 | 0 | |
| Infective enteritis or diarrhoea under 2 years .. .. | 7 | 0 | 0 | 1 | 1 | | 0 | 1 | 0 | 0 |
| Influenza .. .. | 17 | 1 | 0 | 0 | 1 | | 6 | 11 | 3 | 16 |
| Measles .. .. | | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Meningococcal infection .. .. | | 0 | 0 | | | | 1 | 0 | | |
| Pneumonia .. | 510 | 53 | 21 | 13 | 5 | | 46 | 33 | 13 | 19 |
| Poliomyelitis, acute | 9 | 0 | | 0 | 0 | | 0 | | 0 | 0 |
| Scarlet fever .. | | 0 | 0 | 0 | 0 | | 1 | 0 | 0 | 0 |
| Tuberculosis: | | | | | | | | | | |
| Respiratory .. | 93 | 10 | 13 | 0 | 3 | | 2 | 15 | 3 | 3 |
| Non-respiratory | | 1 | 0 | 1 | 0 | | 0 | 0 | 1 | 1 |
| Whooping-cough | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 |
| Deaths 0–1 year .. | 300 | 39 | 38 | 6 | 16 | | 31 | 24 | 7 | 18 |
| Deaths (excluding stillbirths) .. | 10,153 | 920 | 602 | 136 | 180 | | 846 | 680 | 133 | 251 |
| LIVE BIRTHS .. | 13,722 | 1183 | 984 | 239 | 360 | | 1152 | 878 | 218 | 367 |
| STILLBIRTHS | 271 | 21 | 29 | | | | 18 | 24 | | |

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

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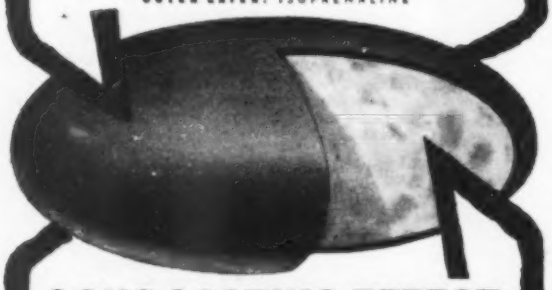

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# Medical News

**Nuffield Committee for the Advancement of Medicine.**—A decree reconstituting the Nuffield Committee for the Advancement of Medicine was approved last week by the Congregation of Oxford University. The object of the change is to meet Lord Nuffield's wishes that the income (about £110,000 per annum) from the trust fund given by Lord Nuffield in 1936 to finance medical research at Oxford University shall be restricted to expenditure on research, including expenditure on the training of postgraduate students in methods of research. The new committee for the advancement of medicine will be composed as before, but its duties will be to formulate policy and to prepare an annual report and accounts for submission to the trustees. The decree adds: "In making such annual reports the committee shall be required to satisfy the trustees that the time spent by the Nuffield professors of clinical medicine, surgery, obstetrics and gynaecology, anaesthetics, and orthopaedic surgery, and by the director of the Nuffield Institute for Medical Research in the instruction for students reading for the degree of B.M., shall not be such as to impair their prosecution of research and of the training of postgraduate students in methods of research." Explaining the new decree in Congregation, Mr. J. C. MASTERMAN said that a smaller special committee would be set up which would have the single function of administering the funds of the benefaction (*Daily Telegraph*, December 3). The proposals have been accepted by the United Oxford Hospitals and by the board of the faculty of medicine at Oxford.

**Travelling Scholarship for G.P.s.**—Details of a travelling scholarship offered by the trustees of the Claire Wand Fund are printed in the Association Notices this week (*Supplement*, p. 254). The purpose of the scholarship is to enable a general practitioner to study what is done for the further education of general practitioners in Canada and the U.S.A. The last date for the submission of applications is January 31.

**Iron in the Home.**—The danger of iron preparations to children in the home is again evident from figures published by the *Pharmaceutical Journal* (November 29, 1958). They refer to England and Wales in 1956 and were specially extracted by the General Register Office. Out of 15 children aged under 5 who died of accidental poisoning, 7 were poisoned by preparations containing iron. By contrast, among the remaining 341 cases of poisoning of persons aged 5 and over none was caused by an iron preparation.

**Mr. H. J. Seddon,** director of studies at the Institute of Orthopaedics, has been elected an honorary member of the Société Française d'Orthopédie and of the Société de Chirurgie de Lyon, having been a corresponding member of both societies for some years.

## NEW ISSUES

*The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.*

**Journal of Neurology, Neurosurgery and Psychiatry.**—Issued four times a year (£3 annually). The new issue, Vol. 21, No. 4, includes:

FURTHER OBSERVATIONS ON SUBARACHNOID HAEMORRHAGE. Wylie McKissock, Kenneth Paine, and Lawrence Walsh.
LEUCOTOMY FOR PAIN. Alick Elithorn, Eric Glithero, and Eliot Slater.
A CONTROLLED STUDY OF THE EFFECTS OF LEUCOTOMY. A. A. Robin.
THYROTOXIC MYOPATHY. Ragnar Hed, Lennart Kirstein, and Curt Lundmark.
INDIVIDUAL VARIATION IN THE SIZE OF THE TENTORIAL OPENING. J. A. N. Corselis.
ARTERIES OF THE SPINAL CORD IN THE CAT. Peter Bradshaw.
ACCOMMODATION IN THE HOLMES-ADIE SYNDROME. G. F. M. Russell.
THE EFFECT OF RESERPINE ON THE DURATION OF MANIC ATTACKS. David C. Watt.
A CONTROLLED TRIAL OF MEPROBAMATE IN ANXIOUS OUT-PATIENTS. John M. Hinton.
MYELOID CELLS IN CEREBROSPINAL FLUID. A. I. Spriggs.
TWO HUNDRED AND ONE CASES OF INTRACRANIAL TUBERCULOMA TREATED SURGICALLY. C. Arseni.

**Journal of Clinical Pathology.**—Issued six times a year (£4 4s. annually). The new issue, Vol. 11, No. 6, includes:

SYMPOSIUM IN HONOUR OF THE CENTENARY OF VIRCHOW'S "CELLULAR PATHOLOGY" (1858-1958):
1858. Sir Roy Cameron.
DIAGNOSIS FROM CELLS. J. Bamforth and G. R. Osborn.
THE BACTERIAL CELL. Robert Cruickshank.
THE CELL IN CULTURE. Honor B. Fell.
CYTOCHONDRIAL ASPECTS OF CELLULAR PATHOLOGY. John W. Harman.
TWO BIOCHEMICAL ASPECTS OF CELL NECROSIS. N. H. Martin.
EXTENSION OF THE LIMITS OF CELLULAR PATHOLOGY: THE ROLE OF ENZYME HISTOCHEMISTRY. A. G. Everson Pearse.
THE EFFECT OF REDUCED OXYGEN TENSION ON PLATELET FORMATION IN VITRO. R. J. V. Pulvertaft.
THE ANTIBODY CONTENT OF SINGLE CELLS. M. C. Berenbaum.
THE CHAIRMAN'S SUMMING-UP. G. J. Cunningham.

**Medical and Biological Illustration.**—Issued four times a year (£3 annually). The new issue, Vol. 8, No. 4, includes:

MYXOEDEMA. J. H. Briggs.
MAX BRÖDEL, 1879-1941. Sylvia Treadgold.
THE ILLUSTRATION OF BRAIN SECTIONS FOR REPRODUCTION. W. Hewitt.
SILHOUETTES. C. E. Engel.
A METHOD OF PRODUCING MODELS OF HOLLOW ORGANS. J. A. E. Gleave
FLASH PHOTOMICROGRAPHY OF LIVING ORGANISMS. B. A. Jarrett.

**Abstracts of World Medicine.**—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

## SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ● Application should be made first to the institution concerned.

### Monday, December 15

GUY'S HOSPITAL.—At Anatomy Lecture Theatre, 5.15 p.m., lecture-demonstration in endocrinology by Dr. P. M. F. Bishop: Anomalies of Sex Differentiation. Guest speaker, Dr. P. E. Polani. A clinical exhibition will be on view before the lecture.
●HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., dinner meeting. 8.30 p.m., discussion: Human Endurance. To be opened by Sir Vivian Fuchs and Dr. O. G. Edholm.
MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Clinical Sciences Building, York Place, 8.30 for 9 p.m., medical film programme.

### Tuesday, December 16

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. J. G. Scadding: Sarcoidosis—Diagnostic Aspects.
ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH.—5 p.m., Sydney Watson Smith Lecture by Professor R. Platt: Some Consequences of Renal Inadequacy.
SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Mr. R. S. Lawrie: Some Surgical Cases.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. L. C. Oliver: Contributions of Surgery to the Treatment and Understanding of Parkinsonism.

### Wednesday, December 17

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Sir John Wolfenden, Kt., Homosexuality and the Law.
BRITISH PSYCHOLOGICAL SOCIETY: MEDICAL SECTION.—At Medical Society of London, 8.30 p.m., papers by Dr. S. I. Abrahams, Dr. V. J. Marmery, Dr. H. S. Pasmore and Dr. M. Balint: The Integrating Role of the General Practitioner.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Guest lecture by Dr. J. M. Barnes: Experimental Study of Toxic Substances.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Epididymitis.

### Friday, December 19

ROYAL MEDICO CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., Professor P. Alexander: Hamlet and the Psychoanalyst.

## APPOINTMENTS

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—Rosalie E. B. Eastwood, M.B., Ch.B., House-physician: V. Ratner, M.B., B.S., Resident Officer to Neurological and Neurosurgical Department; E. P. Berwick, M.B., B.Ch., D.A., Resident Anaesthetist, Tadworth.
LIVERPOOL REGIONAL HOSPITAL BOARD.—Cynthia J. Discombe, M.D., part-time Consultant Pathologist giving six sessions per week to Ormskirk and District Hospital Management Committee group.
WOLLEN, W., M.B.E., Med.Dip., D.P.H., D.P.M., consultant psychiatrist and deputy physician superintendent, Darenth Park Hospital.

## BIRTHS, MARRIAGES, AND DEATHS

### DEATHS

**MacLean.**—On November 10, 1958, at Arichat, Nova Scotia, Iain Malcolm MacLean, M.R.C.S., L.R.C.P., formerly of Isle of Skye, and Sierra Leone, aged 41.
**Male.**—On November 20, 1958, at Dorchester, Dorset, Maurice Taylor Male, M.B., D.P.H., Surgeon Commander, R.N., retired, of Upwey House, near Weymouth, Dorset, aged 83.
**Robb.**—On November 19, 1958, at Western General Hospital, Edinburgh, John Robert Beith Robb, M.D., F.R.F.P.S., B.L., J.P., of Torkillie House, by Carnoustie, Angus, formerly of Lenzie, Dunbartonshire.
**Viasto.**—On November 17, 1958, at "Sherwoods," Hartley Wintney, Hants, John Alexander Viasto, *M.C.*, M.B.
**Wilthew.**—On November 10, 1958, Thomas Nicholson Wilthew, L.R.C.P. &S.Ed., L.R.F.P.S., of Low Fell, Gateshead, Co. Durham, aged 83.
**Wotherspoon.**—On November 15, 1958, at Bow End House, Betley, near Crewe, Cheshire, Allan Wotherspoon, M.B., Ch.B., D.P.H., late of Stoke-on-Trent, Staffs, aged 68.

# Any Questions ?

*We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.*

### Treatment of Diphtheria

**Q.**—*Has diphtheria antitoxin any place in the treatment of diphtheria? How should the general practitioner deal with a suspected case of diphtheria?*

**A.**—Diphtheria antitoxin remains the only specific treatment for diphtheria : antibiotics have little if any place in the treatment. No doctor should take any risks with a suspected case of diphtheria. If the child is croupy he should be sent to hospital, as he needs expert treatment whether the croup proves diphtheritic or not. If a throat swab has been reported positive for diphtheria bacilli the patient should be sent to hospital : if there is membrane in the throat he will be treated urgently as a case of diphtheria ; if there are few clinical signs, he will be isolated for several days until the results of a virulence test are known. If the patient has exudate on the throat which the general practitioner thinks might be diphtheritic, he should try to get the advice of a consultant from an infectious diseases hospital—the only person likely these days to have clinical experience of diphtheria. If admission to hospital is not arranged, a throat swab for organisms and blood for white cell count and Paul–Bunnell test should be sent to the laboratory. Infectious mononucleosis is the commonest cause of membrane in the throat resembling diphtheria. If the degree of suspicion is high enough to suggest giving antitoxin, then not less than 20,000 units should be given—this is an adequate therapeutic dose for a mild case of faucial diphtheria. But if antitoxin seems necessary, admission to hospital is even more necessary.

### Cushing's Syndrome

**Q.**—*How can one differentiate between the pituitary and adrenal types of Cushing's syndrome?*

**A.**—The clinical features of these conditions are described by some as Cushing's disease and Cushing's syndrome, respectively, to denote the so-called pituitary and adrenal types. More generally the term Cushing's syndrome is used in the description of the whole group. It seems certain that in all instances there is increased formation of cortisol by the adrenals, and this is of the greatest importance in the production of the clinical features. The adrenals may be of normal size or, more usually, hyperplastic and occasionally the site of an adenoma or carcinoma. A patient with a tumour may occasionally be distinguished clinically by the additional presence of signs of virilization.

It is widely assumed that all the non-tumorous adrenals are stimulated by excess of secretion of corticotrophin by the anterior pituitary, but this has been shown to be true in only some and not all of the few cases examined. Sometimes small basophil adenomas are present in the pituitary but are not large enough to be detectable by clinical means. Rarely, larger basophilic or chromophobe tumours are found, sufficient to produce local radiological abnormalities or even an occurrence of visual changes due to chiasmal pressure. If such changes are present the pituitary can definitely be incriminated. More usually the problem resolves itself into an attempt to demonstrate the presence of an adrenal tumour, and this may be based on some or all of the following observations: (1) Abnormal renal position shown by I.V.P. (2) Outline of tumour by presacral air insufflation. (3) Excess excretion of adrenal corticoids with notable increase of 17-ketosteroids. (4) Poor response of corticoids to corticotrophin stimulation together with absence of significant diminution after the administration of suppressing steroids such as 9$\alpha$-fluorohydrocortisone. (5) The presence of secondary growths (although here care must be taken to distinguish those occasional cases of Cushing's syndrome associated with bronchogenic carcinoma). (6) Operative demonstration of a tumour.

The practical importance of making the questioner's differentiation is that tumours of the adrenal should always be removed if this is possible. In some cases where it is thought that the pituitary is excessively stimulating the adrenal, it may be desirable to treat by local application of $\beta$ radiation, proton bombardment, $x$-irradiation, or possibly by hypophysectomy, rather than choose the alternative of subtotal or total bilateral adrenalectomy.

### Nystagmus

**Q.**—*In the absence of organic disease, can nystagmus be present in a person who is not under the influence of drink or drugs?*

**A.**—Congenital nystagmus can occur in the absence of any demonstrable lesion of the visual system or of the vestibular nerves and their central connexions. It is usually a rapid, pendular movement, sometimes associated with movements of the head. The condition may be present in several members of the same family. Hysterical nystagmus is said to occur, but the writer has never seen it. The tale is told of a medical student who was able to astonish his teachers by the voluntary production of nystagmus.

## NOTES AND COMMENTS

**Barbiturate Chemistry.**—Mr. H. H. ARMSTRONG, F.R.I.C. (Stockport), writes: May I draw your attention to an error of chemical nomenclature (*Journal*, November 29, p. 1347)? Barbituric acid is classified as a diureide, whereas it is, in fact, a cyclic monoureide. It is further suggested that the reaction for the formation of barbituric acid should show the working conditions—i.e., phosphorus oxychloride and 100° C.

**Disclaimer.**—Mr. B. W. RYCROFT writes: My attention has been drawn to an article which was published in a Sunday newspaper on November 9, in which my name and those of my staff were mentioned. Would you please be kind enough to inform our profession, through your columns, that this article was published entirely without my knowledge, approval, or consent, and that no information was supplied to the newspaper by any member of my staff.

**Corrections.**—In the article on "Onset Enuresis" by Drs. J. D Paulett and E. Tuckman (November 22, p. 1266) the word "unreasonably" appeared instead of "unreasoningly" in the sixth line of the right-hand column on p. 1267.

In the article on "Drugs in Treatment of Epilepsy," by Dr. D Williams (*Journal*, November 8, p. 1155) the long-acting phenobarbitone should have been described as in "spansule" form, not "enseal."

**Collected Articles from the "British Medical Journal"**

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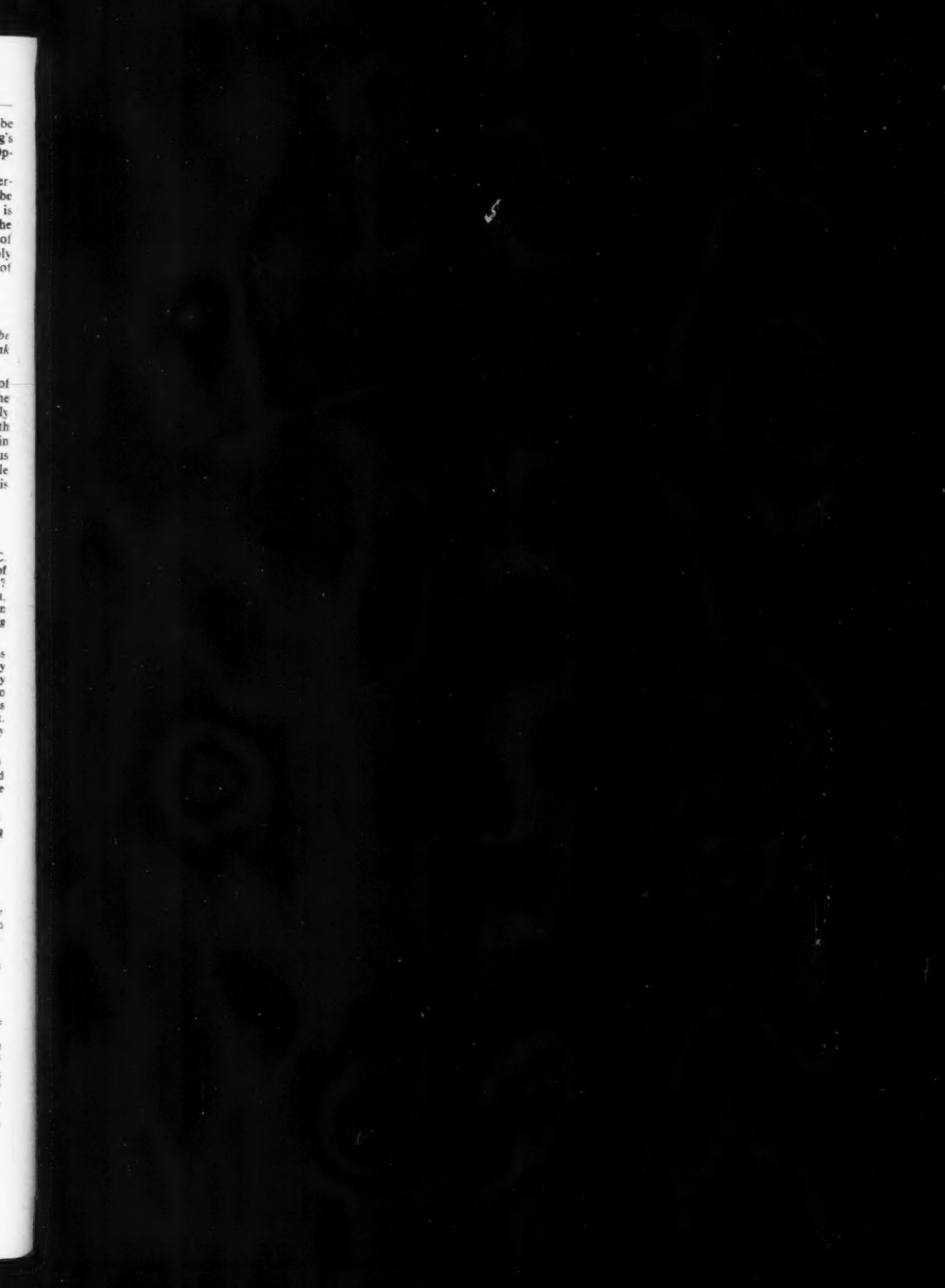
*Any Questions?*, Volumes 2 and 3 (8s. 3d. each).

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